

that time), but both examples illustrated are typical. The first, showing a huge meningocele, has obvious lacunae in the vault bones, whilst the second shows them together with craniostenosis, but they are not referred to in the text. Shanks, Kerley and Twining, a three volume modern treatise on Radiology, mentions Luckenschädel and dismisses it very briefly as a form of craniostenosis, making no mention of its association with spina bifida or any other deformity, or of its existence independently from craniostenosis.

CASE RECORDS

The first case which attracted our attention was noteworthy in that, for the first time, the diagnosis was made before birth, radiologically. Our investigations were centred on this case, which we therefore report in detail. Subsequent cases are reported more briefly.

CASE 1 The mother Mrs W H was a primigravida aged 23 years, who came from a healthy family. Her mother and two sisters had had several pregnancies but no stillbirths. Their children had no deformities none had died at an early age and none was mentally abnormal. The female relations of her husband gave similar histories. The patient herself was a well-built girl with no evidence of congenital abnormality nor of rickets. She had had scarlet fever at 9 years of age and an appendicectomy performed at 18 years of age. Her husband had a marked scoliosis but was otherwise healthy. Radiographs of both parents' skulls were taken and both presented normal appearances.

The mother attended the antenatal clinic regularly and appeared to be a normal case until October 9th 1941 in the 36th week of pregnancy when it became apparent that she had developed hydramnios. This was not excessive and the foetus could still be palpated being found to lie in the right sacro posterior position. The foetal heart sounds could be heard and there was no evidence of pre eclamptic toxæmia.

A radiological examination was made, the presentation was confirmed, and craniolacunia and spina bifida found to be present. Our reading was as follows:

October 9th 1941 'Single foetus, breech in RSP position with extended legs. Gross deformity of the lumbar spine, and abnormality of development of the frontal area of the skull. Probably a case of Luckenschädel with spina bifida. Normal maternal pelvis' (J B H)

A low surgical rupture of the membranes was performed on October 16th, 1941, and 2 days later she gave birth without difficulty to a stillborn female child, which was delivered as a breech with extended legs. The foetal heart sounds were heard during the 1st stage of labour which was prolonged, but not following full dilatation of the cervix. The placenta was born 5 minutes after the foetus and appeared to be quite normal. The whole labour lasted 40 hours.

Wassermann tests were performed on the maternal and on the foetal blood and both were negative.

The child was a female of calculated maturity of 37 weeks. Her weight was 4 pounds 14 ounces and its length $17\frac{1}{4}$ inches. The head was not unduly large and its circumference measured around the occipito-frontal diameter was $12\frac{1}{2}$ inches. The sagittal metopic, coronal and lambdoid sutures were still open and measured $\frac{1}{4}$ inch in width. The posterior fontanelle was still present and the anterior fontanelle measured $1\frac{1}{2}$ inches long by 1 inch wide. Foramina depressions or ridges could not be felt in the bones of the cranial vault.

The lower dorsal and lumbar spine showed marked abnormality, a large myelocoele being present. There appeared to be failure of fusion of the neural arches of the 9th dorsal to the 2nd lumbar vertebrae, the bodies of which formed an angular lordosis. The cord lay exposed in the hollow of the lordosis entirely bereft of superficial covering with the central canal opening into the upper part of the exposed area.

An incision was made in the sagittal plane of the skull and the cranial vault with the dura mater attached was freed from the underlying brain. Lacunar depressions were immediately noticed on the inner surface of the cranial bones and the relation of these to the surface of the brain

was observed. It soon became apparent that there was no relation between the ridges and depressions on the cranial bones, and the sulci and convolutions of the brain. *In no area did the cerebral convolutions fit into the bony depressions.* The meningeal and cerebral vessels similarly bore no relation to the network of bony ridges, the brain in fact was normal, the ventricles were not dilated and the cortex was not thinned.

The cranial bones were carefully removed from between the pericranium and dura mater, and studied in some detail. The same changes were found to affect the parietals, frontals and the squamous portion of the occipital bone; they were present, although to a lesser degree in the squamous portions of the temporal bones and the great wings of the sphenoid. Externally these bones were of normal smoothness, but their internal surfaces were marked by a network of bony ridges which enclosed circular and oval areas of very thin bone, measuring $\frac{1}{2}$ to 1 cm in diameter, while in some of these areas, ossification of the membrane had not occurred, and true foramina were present. The bony configuration thus produced did not resemble the cerebral pattern of gyri and sulci but was an independent design of contiguous circles and ellipses. This was best shown in the frontal and parietal bones (Fig 1).

The remaining organs of the foetus appeared normal. There was no clubbing of the feet and no congenital heart disease. The endocrine glands including the suprarenals appeared normally developed. (Observations of C W F B at post mortem.)

The radiological features of this case were

(a) Those already described in the report on the foetus *in utero*, i.e. the defect in the cranial bones and the deformity of the spine (Fig 2)

(b) Those of the stillborn foetus which were

1 The typical defective ossification shown by the dense bony bars and the contrasting lacunar areas, these changes being confined to the frontal and parietal bones, and the squamous portion of the occipital

2 Absence of recognizable sutures in the cranial vault

3 Prominence of the frontal region with relative depression of the bridge of the nose. Deep and large orbital fossae. The bones of the base of the skull were apparently normally developed.

The spheno-occipital 'suture' presented normal appearances and the space normally visible at term between the squamous occipital and the ex-occipitals in the lateral view of the skull, was also present and of normal width.

4 Deformity of the spine resulting from extensive and gross failure of normal development of the lower four dorsal and upper two lumbar vertebrae. The cervical spine was normally developed. The spine below the 2nd lumbar vertebra presented a return to normal appearances of the individual vertebrae except that the lumbar spine as a whole was of such dimensions that it resembled a sacrum. There were 12 ribs on the right side. On the left side the 3rd rib and the head of the 8th were defective, while the 9th, 10th, 11th, and 12th were represented by a single deformed unit.

All the long bones, the pelvis, both scapulae and both clavicles exhibited normal appearances for a foetus of this age (Figs 3a and 3b).

(c) The contrasting appearances of these craniolacunar vault bones when radiographed side by side in the dried state, with bones from a normal foetus of the same age (Fig 4). The striking features on comparing the appearances of these sets of bones are the changes in organized pattern of the bony detail and the difference in the bony outline. In the normal skull the trabecular pattern radiates from a point at or near the centre of the bone finely and evenly in all directions to the periphery, whereas in the craniolacunar bones, particularly the frontals and parietals, this

pattern is almost completely lost. The bone edges in craniolacunia are ragged and irregular in striking contrast to those of the normal skull bones. Superimposed upon the exceedingly fine pattern of trabeculation, the bars and lacunae of craniolacunia are very evident. It also becomes apparent that the squamous temporals share in the craniolacunar changes, although this fact is not demonstrable in the radiograph of the intact foetal skull. It is in the deposition of the bone that the abnormality lies, where bone has been laid down it tends in general to be of normal density.

The vault bones shown in Figs 1 and 4 from two foetuses of the same age were weighed. These weights are given in the following table.

Bones	Weight of normal	Weight of craniolacunar	Per cent of normal
Frontals	2.25 gm	1.18 gm	52.4
Parietals	3.57	2.21	61.9
Squamous occipital	2.45	1.48	60.4
Total	8.27 gm	4.87 gm	58.9 per cent

CASE 2 The mother, Mrs N S, aged 27 years, was a primigravida who gave birth normally to a female stillborn child at term on November 4th 1941.

The child had a large meningocele present in the lumbar region associated with talipes of both feet. Radiographs of the skull revealed the presence of craniolacunia with raggedness of the posterior margins of the frontal bones and anterior margins of the parietals while irregularity of bony density and the lacunar defects were also evident in these bones. The wide sutures were clearly visible and the bones of the base of the skull and face were normal. The whole of the dorsal spine showed a condition of spina bifida; the upper six pairs of ribs were deformed; there was a sharp kyphosis and scoliosis in the lumbodorsal spine and in the upper lumbar region there was gross developmental defect in the formation

of the vertebral bodies. The long bones and pelvis showed no abnormalities of development or structure.

Review of the antenatal radiographs of this stillbirth in the light of our investigation of Case 1 showed that the associated skull defect and spinal deformity were there demonstrable.

CASE 3 G R was a living male infant born November 2nd, 1941 as the second of twins. His brother appeared healthy and weighed 5 pounds 7 ounces whilst he himself had an occipital encephalocele of practically the same size as the head and weighed 7 pounds 4 ounces. His skull was the smaller of the two and had a markedly simian appearance while the bones of the vault X-rayed 24 hours after birth showed typical craniolacunia of a mild degree. The bones of the face and of the base of the skull were normal. There was no

bulging of the sutures which were $\frac{1}{4}$ inch in width and the anterior fontanelle was slightly larger than that of his twin (Fig 5). No defects were detected in the remainder of the skeleton.

The skull of the twin brother was normal in size and shape. The bones of the base, the facial bones, the frontals and the squamous occipital were normal in appearance. The lateral radiograph showed a small area of abnormal ossification in the upper parietal region but no true craniolacunia. No defects were detected in the skeleton radiologically.

CASE 4 H S was a full term male born October 31st 1941 weighing 7 pounds 8 ounces and exhibiting a sacral myelocele. Radiographs 8 days after birth did not show any deformity of the spine or skeleton apart from the lumbosacral spina bifida. The bones of the vault of the skull

showed mild but definite craniolacuniae with the posterior margins of the parietals extremely irregular and the coronal and lambdoid sutures very wide but not bulging. The space between the squamous occipital and the exoccipitals was normal in width and definition.

CASE 5 S R was a female born November 11th 1941, at term with small meningoceles in the mid-dorsal and lumbar areas and with paralysis of the left leg. She was referred for X-ray examination of the spine on November 15th, 1941, abnormality of the skull not having been noted clinically. Fortunately the radiographs included the skull. They revealed well-marked craniolacuniae, the facial bones and those of the base of the skull being normal whilst the bones of the vault showed typical bars and deep lacunae. In contrast to the previous cases described, the fontanelles were almost closed and the sutures were detectable only on close examination. The upper six cervical vertebrae were correctly formed but the 7th cervical vertebra and the whole of the dorsal spine showed gross deformity (scoliosis and kyphosis) the development of the individual vertebrae within these limits being completely chaotic.

Radiographs obtained 5 months later, a few days before death occurred, showed that the contrast between bars and lacunae had distinctly diminished in spite of the enlargement of the head which had taken place, whilst the sutures were enlarged as compared with the original size, there being thus a definite suggestion of concomitant diminution of the craniolacuniae, together with the development of a degree of hydrocephalus.

CASE 6 This child H H, a living male, was admitted to hospital on December 5th, 1941 having been born at term that day in the district.

It was sent because it showed (1) Extensive spina bifida with myelocoele (2) Gross deformity of the dorsal spine (3) Bilateral talipes equinovarus (4) Deformity of the penis and of the nose.

It was referred for X-ray examination of the spine only but the whole child was radiographed.

Study of the films revealed (a) Mild craniolacuniae with deficient ossification of parietals, normal ossification of the base, and normal sutures and fontanelles (b) Skull of normal size and shape (c) Gross dystrophy of the dorsal spine with spina bifida in the lumbar and sacral regions.

CASE 7 The mother, Mrs A B was delivered at term (December 24th, 1941) of a stillborn male child whose skull being markedly hydrocephalic had required perforation to effect delivery. Examination showed the bones of the vault to be larger than normal, with ragged edges and gross craniolacuniae the lacunae being very poorly ossified with many areas of total bony deficiency (fenestration). These features are clearly shown in the photograph of the dried vault bones (Fig 6). There were also spina bifida and a myelocoele in the lumbar region of the spine.

Radiographs of this foetus demonstrated typical lacunae in the vault bones of the skull, whilst in the spine and ribs several abnormalities were seen. There were six cervical, 12 thoracic, 6 lumbar and 5 sacral vertebrae, all their bodies were distinct and normally formed, but there was spina bifida from the mid-dorsal region downwards. The 4th right rib was broad, and it bifurcated from its mid point, while the 5th showed a deformity of its head and neck.

X-ray films obtained by the use of Grenz rays (Fig 7) demonstrate strikingly the extent and degree of faulty ossification of the dried, disarticulated frontal and parietal bones and the squamous occipital. Comparison with Fig 4 shows the exaggerated form of craniolacuniae which may occur in the bones of the hydrocephalic skull.

CASE 8 J B was a living female child delivered December 15th 1941, at term. The sutures of the skull were $\frac{1}{4}$ inch in width and the fontanelles were large although there was no suggestion of hydrocephalus. Spinal deformity or other skeletal defect was not apparent. Radio-

logical examination of the skull revealed the appearances in the bones of the vault of a mild form of craniolacunia. The bars were not thick and the lacunae were relatively shallow, but the pattern was quite unmistakable. The spine was normal.

CASE 9 The mother Mrs V S, was a primigravida aged 22 years, who was referred to one of us (J B H) for radiological investigation on February 4th 1942 the foetal head having failed to descend into the pelvic inlet.

The radiological report was 'There is a single foetus which shows gross deformity of the spine and is in danger of presenting as a brow or a face. I think there is slight hydrocephalus. In addition the skull bones are not of normal density and I strongly suspect that this foetus will be found to show craniolacunia associated with spinal deformity and either encephalocele or meningocele or myelocele. I would very much welcome the opportunity of X-raying this foetus after delivery.'

At delivery, February 24th, 1942, the hydrocephalic skull was perforated and a female foetus showing complete lumbar spina bifida was born.

Clinical examination of the skull bones after removal of the brain showed the usual smooth outer surfaces of all the bones of the vault, while on the inner surfaces, the bars and lacunae were clearly to be felt and seen.

Radiographs of this skull demonstrated the typical appearances of craniolacunia without the very marked fenestration which was exhibited in the vault bones of the hydrocephalic foetus in Case 7. The deformity of the lumbar spine corresponded accurately with that revealed in the antenatal radiographs of this foetus, there being well marked kyphosis of the lumbar spine, while both the lumbar region and the sacrum showed spina bifida.

CASE 10 The mother, Mrs L W, was a primigravida aged 30 years admitted February 23rd 1942 suffering from eclampsia.

On February 25th 1942 (i.e. in the 34th week of pregnancy) she was delivered of a male stillborn

hydrocephalic foetus, weighing 4 pounds 15 ounces. There was no other skeletal deformity to be seen clinically.

Radiologically gross hydrocephalus was confirmed with craniolacunia which, although not as marked as in Case 7, was quite typical except that, owing to the gross hydrocephalus, demonstration of the margins of the bones of the vault was not successful until they had been disarticulated and dried. There were found also bilateral cervical rib, deficiency of the 3rd right rib, and defective development of the 1st and 2nd dorsal vertebrae. Neither the lower femoral nor the upper tibial epiphyses were visible.

CASE 11 The mother Mrs E G, aged 25 years was delivered on March 10th, 1942 normally, at home of a living female child weighing 8 pounds, which was admitted to hospital because of spina bifida and a discharging lumbar meningocele. By chance the existence of this child in the ward was discovered by one of us and the whole child was examined radiologically. Well-marked craniolacunia was revealed the bars and lacunae being well developed. The fontanelles were large and all the sutures were wide. The margins of the vault bones were not as irregular as those seen in hydrocephalus of which there was no suggestion here.

The difficulties of obtaining first-class radiographs of a living infant of this age by means of a mobile ward unit, which was all that was available in this instance, will be appreciated. Nevertheless, the dorsal spine as far as the 11th vertebra appeared to be normally developed. In the lumbar region there was slight but definite kyphosis and scoliosis and there was clearly visible the lumbar meningocele, measuring 5.5 cm transversely, 5.2 cm in length and projecting backwards for 2.5 cm.

This mother gave an interesting obstetrical history thus 6 years ago, spontaneous

miscarriage at 4 months, 4 years ago, delivery of normal living female child by the forceps, 15 months ago, induction at 7½ months of an anencephalic foetus

DISCUSSION

It is remarkable that this sequence of 11 cases of craniolacunia should have occurred in our hospitals during a period of 5 months, considering that only one case has been reported in this country since 1875, and it has provided us with much material for investigation. In addition to this series, we have found 2 more cases of craniolacunia illustrated in books, yet remaining undetected, and we continue to discover other examples whenever old pregnancy radiographs come up for review. Two requests to neighbouring obstetricians to send their next cases exhibiting spina bifida to us for investigation, resulted in the demonstration of craniolacunia of obvious degree in each case.

We estimate that the condition is appearing at present in 0.8 per cent of all births, having found 5 examples occurring in 600 deliveries at one hospital during the period of our investigations. We thus support Vogt and Wyatt's estimate, which was based on an examination of 6,000 skulls of infants, and which also placed the incidence at 0.8 per cent.

We suggest that radiological examination of the skull should be carried out in addition to radiography of the spine, in all cases of spina bifida and hydrocephalus. Three of our series (Cases 1, 2 and 9) show clearly that antenatal radiological examination does enable the diagnosis to be made before delivery provided that the radiologist is aware of the significance of the abnormalities revealed. It is certain that careful examination of routine pregnancy radiographs and radiological examination of the skulls of children exhibiting spinal

defects will demonstrate the comparatively high incidence of craniolacunia.

The theories which have been advanced in the past by various authors to account for craniolacunia can be broadly classified into the three following groups:

Group 1 Theories of inherent developmental defect

Group 2 Theories of causal disease

Group 3 Theories of pressure disturbance

Evidence derived from the study of our series of cases throws considerable new light upon these earlier theories. Thus we are unable to support Engstler's proposition that the developmental defect is due to the diminution of blood supply resulting from occlusion of the vertebral arteries. We can find no evidence that this occurs, and moreover it would not explain the frequently associated spinal defect. Cohn, who first reported the existence of craniolacunia in normal infants, maintained that it was merely a manifestation of delayed development in such cases. Vogt and Wyatt also reported two such examples. We agree that it does exist in otherwise normal infants (as in Case 8), but it cannot be an expression of delayed development, because the bars and ridges of a craniolacunar skull in a foetus of 8 months (Case 1) were thicker than the bones of the normal skull at term. It is thus a disorder of development and not a simple underdevelopment.

All observers have stressed the frequent association of craniolacunia with other developmental defects such as talipes and spina bifida which may be either myelocoele or meningocele, single or multiple, small or large, and may occur in any region of the spine. Encephalocoele is also described. Doub and Danzer alone have recorded the presence of deformed ribs in a single instance. All these types



FIG. 2

Radiograph from Case 1 showing clearly the spinal deformity and defective ossification of the bones of the vault which enabled the mitral diagnosis of craniocervical to be made.



FIG. 3

Photograph of the dried vault bones from Case 1 showing well marked craniocervical beside those of a normal foetus of the same age.



Fig. 31

Lateral radiograph of the stillborn foetus



Fig 3b

A P view of this foetus. Confirming the presence of craniolencia
and the spinal defect

H & B

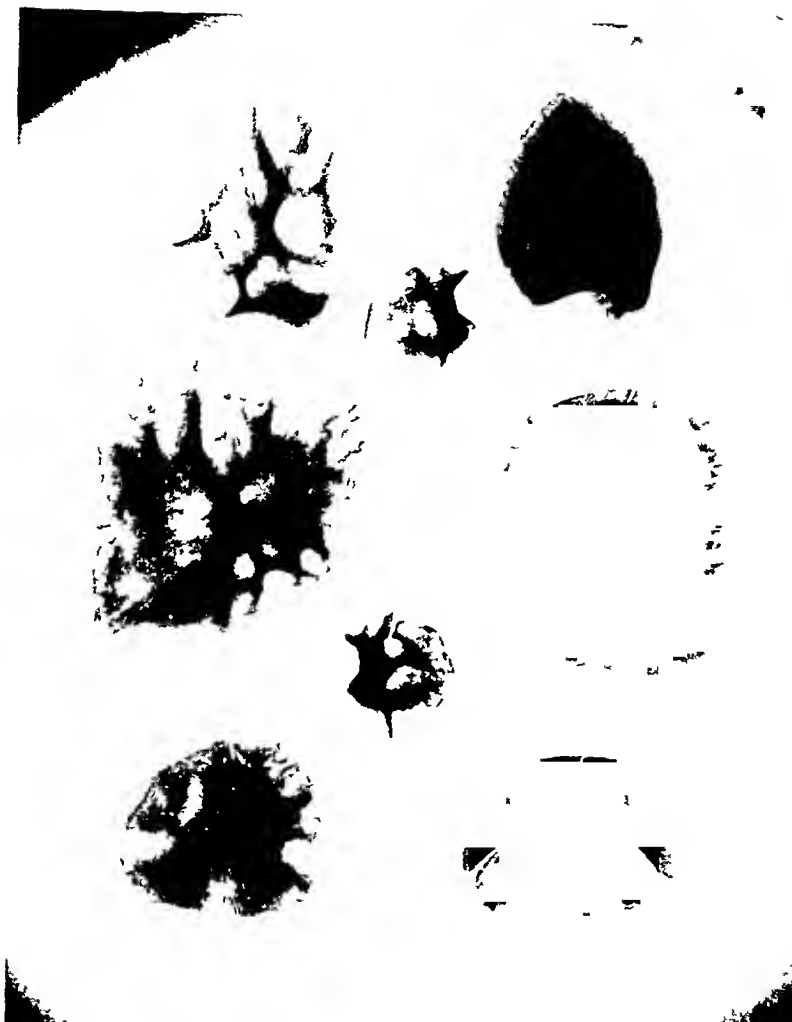


FIG. 4

Contrasting radiograph of the dried skull bones seen in Fig. 1 showing the normal structure of the vault bones at 37 weeks as compared with the faulty architecture seen in cranioleukia at the same stage of development

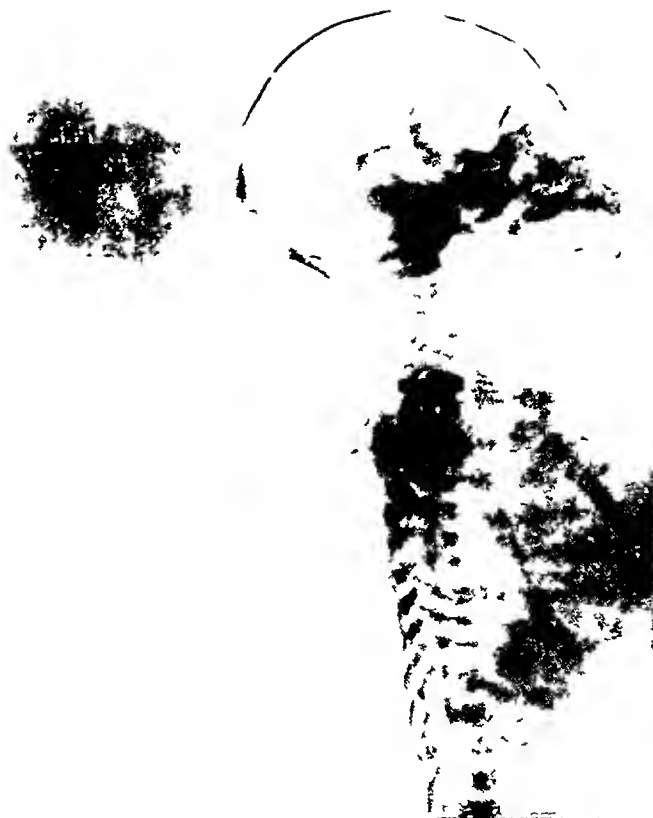


FIG 5

Lateral radiograph of Case 3 showing craniocle and well marked craniocle

H & B



Fig. 6

Photograph of the dried vault bones from Case 7. The frontal bones in parietal and the parietal bones to a lesser extent show the extreme degree of the anomaly which we propose to call *anomalocystis*.

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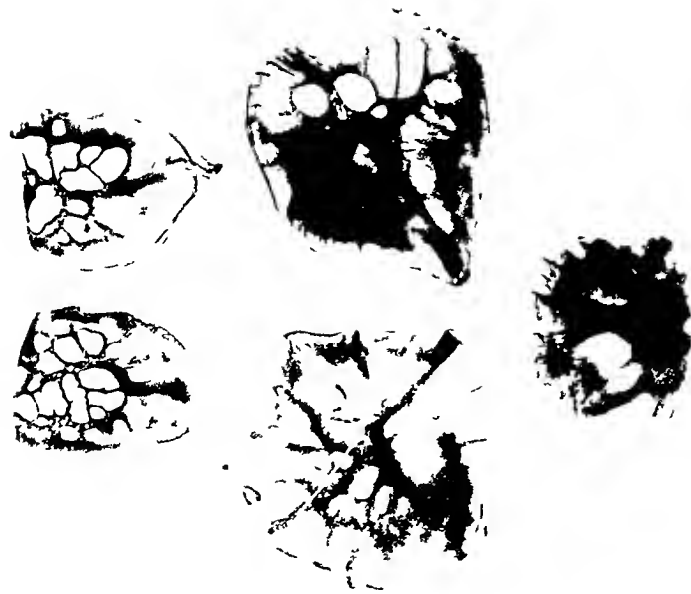


Fig. 7

Photograph of the dried vault bones from Case 7 which shows even more strikingly than in the photograph (Fig. 6) the extent and degree of development of deficiency which can appear when a malocclusion and hydrocephalus are associated.

of defect have occurred in our series. Thus myeloceles were present in Cases 1, 4, 6 and 7, and meningoceles in Cases 2, 5 and 11. The spine of Case 10, which clinically did not show any sign of abnormality, was shown radiologically to be defective in the development of the bodies of its 1st and 2nd dorsal vertebrae, which had been formed from two centres of ossification which had failed to fuse centrally. Case 8 alone was free from any spinal defect. Case 3 exhibited a large occipital encephalocele, while the detection of rib deformities in 4 of our cases (1, 2, 7 and 10) has enabled us to confirm Doub and Danzer's original observation. Talipes, frequently reported by early observers, was present in Cases 2 and 6, while two deformities hitherto unrecorded in the literature, namely hypospadias and malformation of the soft tissues of the nose (the nasal bones, maxillae, and others being normal), were seen also in Case 6. Sear¹² has shown that cranio-lacunia is frequently present in cases of the rare condition cranio-stenosis. None of our series demonstrates this association and in fact the only example of cranio-stenosis which we have encountered during this investigation, which was incidentally, a cyclops, was devoid of the lacunar changes. We agree with Vogt and Wyatt that the frequency with which these apparently developmental anomalies are associated with cranio-lacunia does support the view that they may all result from an inherent developmental defect, which mainly involves the various parts of the enfolding mesoblastic layer of the skull and spine.

Few authors have supported the theory of a disease process being the causative factor. Hughes alone has suggested that rickets and syphilis might be responsible, while some German authors have favoured syphilis. Doub and Danzer, who based their report on the Wassermann test of two

mothers, rejected this contention. Obstetrical histories, clinical examinations and blood tests on mother and child have made us do likewise, furthermore radiological examination of the skulls of known syphilitic infants has not once revealed the presence of cranio-lacunia. We have not found any clinical or radiological evidence of rickets in any of our cases. We have investigated questions of heredity, the age and degree of parity and general health of the mother, and find that none of these has any bearing on the aetiology. In our series there were 5 males (of which 2 were stillborn) and 6 females (of which 3 were stillborn) so that neither the sex of the infant nor foetal mortality is of significance. Pre-eclamptic toxæmia had no relation to the condition, 10 of the pregnancies being free from toxæmia, and one having fully developed eclampsia. Hydramnios is well known to accompany foetal deformities so that its occurrence in our series is not surprising. Thus we have not found any evidence to suggest that disease plays any part in the causation of cranio-lacunia.

The explanations of the lacunar changes in the vault bones of the skull which have attracted the greatest number of adherents, are those based upon the supposition of abnormal pressure bearing upon the developing skull, either from without or from within. Kassowitz, who advanced the theory of external pressure, considered that it was exerted on the skull during labour and was sufficient to account for the changes observed. Although finding no supporters, this suggestion has never been rejected, because the diagnosis of cranio-lacunia prior to delivery had never been made. Our series finally disposes of this theory, since the definite antenatal diagnosis was made in Cases 1 and 9, 4 weeks and 3 weeks respectively before the calculated date of delivery.

The theory of increased pressure upon the bones from within, by means of an increased intracranial pressure, was accepted by many authors, from Von Recklinghausen in 1886 to Shearer in 1937, and was based on the pure assumption that the lacunae corresponded to and were produced by the cerebral convolutions, and that they were analogous to the "thumbing" which has been so widely accepted in the past as evidence of internal hydrocephalus. Superficially this explanation appeared to be reasonable, especially as the frequent association of cranio-lacunaria with spina bifida suggested the dual result of internal pressure effects and Faust even suggested that the cerebro-spinal fluid drained away from the brain through the spinal defect and thus allowed the convolutions to exert excessive pressure on the developing skull. The not uncommon finding of hydrocephalus, mentioned by Doub and Danzer, and wide sutures and large fontanelles in cases of cranio-lacunaria appeared to support this view. Not until 1941 was doubt thrown upon this theory, when Vogt and Wyatt questioned the possibility of the developing infantile brain, which is gelatinous in consistence at this age, causing convolutional impressions in the skull bones. Our findings in Case 1 completely disprove this theory, because at postmortem it could be seen that the gyri did not fit into the lacunae, the bony bars were crossed at all angles by the convolutions and the two patterns were entirely dissociated. Furthermore, there was no evidence of increased intracranial pressure having existed, and the ventricles presented normal appearances. Detailed study of the skull bones and their radiographs (Figs 1, 4, 6 and 7) shows that there is not any constant lacunar pattern in the corresponding bones of different cases, such as one would expect if the lacunae were produced by the convolutions.

The analogy to "thumbing" of the skull we believe to be incorrect. In this condition bony bars of more than normal skull-thickness are never produced, and the depressions never disappear when once formed, whereas the lacunae, as we have observed in Case 5, were becoming less obvious within 5 months of birth. Vogt and Wyatt state that the latter were often obliterated after one year. Moreover it is quite erroneous to regard "thumbing" as evidence of increased intracranial pressure, precisely because it can be shown to be as marked in some normal individuals as in cases of proved raised intracranial pressure. Indeed in the latter evidence of "thumbing" may be completely lacking. Increased intracranial pressure cannot be the common cause of wide sutures, large fontanelles and cranio-lacunaria, because although they are often found in association (Cases 1, 2, 3, 4, 8 and 11), cranio-lacunaria does occur when the sutures are small (Cases 5 and 6) and even when they are prematurely closed as in cranio-stenosis, as Sear has shown. American writers stressed the frequent combination of cranio-lacunaria and hydrocephalus, Doub and Danzer expressing the view that they were usually found to co-exist. In our own series of 11 cases 3 were hydrocephalic (Cases 7, 9 and 10). We consider this to be the only evidence which supports the theory of increased intracranial pressure as a causal factor, but even this we do not accept, because examination of other hydrocephalic skull bones has failed to reveal any evidence of cranio-lacunaria. Thus the theories which account for the occurrence of cranio-lacunaria by alterations of pressure, although ingenious, are not supported by careful post-mortem findings, or by recent evidence.

It is strikingly apparent that the cranio-lacunaria occurring in Case 7 is of a more pronounced character than that present in

our other cases. Complete defects of ossification preponderate, with the result that actual perforations covered by membrane are more frequent than lacunae. This is well shown by comparison of Figs 1 and 4, and 6 and 7. The bony bars which slope gradually into the lacunae pass abruptly into the perforations which are characteristic of Case 7, thereby producing a punched-out appearance. We feel that a separate name should be applied to this exaggerated form of craniolacunia, and we therefore suggest the term *craniofenestria*. It will be seen from Figs 6 and 7 that this *craniofenestria* is most extensive in the frontal bones, less so in the parietals and least of all in the squamous occipital.

We suggest that the inferences we have drawn from the material already at our disposal have been sufficient to eliminate most of the previous theories, which have produced a confusing picture in the literature. So far, we cannot confidently replace them with an alternative. We have been unable to discover any causal disease and an abnormal pressure we consider to be most unlikely. Craniolacunia must, we feel, be due to a developmental defect in which two processes are frequently associated, namely the faulty ossification of the primitive membranous vault which surrounds the early brain, and the faulty chondrification of the vertebral bow of the primitive membranous spinal column which surrounds the early spinal cord. Why should this defective formation occur? It may be due to an inherent defect of a chromosomal nature in which unhealthy mesodermal tissue is produced. In this case one might expect to discover evidence of its transmission from parents to offspring. Spina bifida is not a defect which can be handed down to the progeny (except in rare cases of successful operation or in spina bifida occulta), but craniolacunia alone might be so transmitted. It is too

early to have seen examples of this, and it is doubtful if it does occur, because as far as we can discover, successive children of the same parents are not afflicted with either of these conditions. Like so many anomalies, its cause must at present remain obscure, factors such as calcium or phosphorus deficiency, abnormal metabolism, hormonal imbalance or toxic process may quite well play a part, but at present we do not have any exact knowledge. It is evident that there exists a large field for future research towards the elucidation of this problem.

SUMMARY

1 Eleven new cases of craniolacunia are reported.

2 The incidence rate is shown to be vastly greater than hitherto suspected in this country and to equal that recently demonstrated in America.

3 The actuality of antenatal radiological diagnosis is emphasized.

4 Most of the previous theories regarding aetiology are shown to be incorrect, and lines of future research are indicated.

5 The term *craniofenestria* is suggested for the more severe form of craniolacunia which exhibits areas of totally defective ossification.

ACKNOWLEDGMENTS

Our thanks are due to Miss Marsden of the Christie Hospital and Holt Radium Institute, Manchester, for the photographs of specimens, and to Mr A. V. Gill of Kodak, Ltd., for advice in the preparation of the contrast radiographs of foetal skull bones, while Dr Malloch, Resident Obstetrical Officer at the Lake Hospital, Ashton-under-Lyne, kindly afforded us facilities for the study of the foetus reported in Case 9.

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Maternal Birth Palsy due to Trauma

BY

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MATERNAL birth palsy due to trauma is a rarely reported complication of labour. The paralysis affects part or parts of the lower limb of the mother, appears early in the puerperium or during labour itself, and is caused by trauma to the nerves traversing the pelvis, more commonly the sacral plexus.

As long ago as 1838, von Basedow¹ described such forms of paralysis. Later it was described in the French literature by Bianchi² in 1867, and Lefebvre³ in 1876. The most quoted paper on the subject, and the first to give a satisfactory explanation of the origin of the paralysis, is that of Hunermann⁴ in 1892.

The number of the reported cases of the condition is small and many textbooks on obstetrics make no reference to the complication. Tillman⁵ reviewed the literature, collected and analysed 107 cases, and added 8 of his own.

It is interesting to note that the lesion is known to occur in animals as well as in the human. Craig⁶ says, "Paralysis after parturition may be occasionally noted in any of the domesticated animals, but it is most frequent in the cow."

During the last 12 months we have had 3 mothers with traumatic birth palsy at University College Hospital.

CASE 1 (G 206) Age 33, 5-para. This patient's previous pregnancies had all been uncomplicated. The largest infant had weighed 9 pounds 5 ounces

and was the outcome of her second pregnancy in 1933. The present pregnancy was normal.

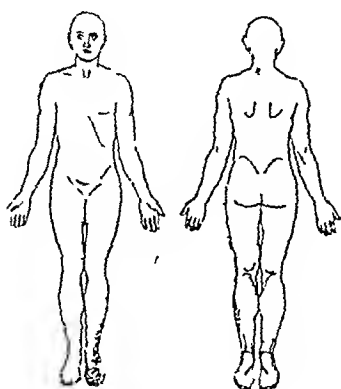
She was admitted to hospital in labour at term at 10 p.m. on April 7th 1941. Her pains had begun at 5.30 p.m. that afternoon. The foetus was presenting by the vertex which was above the brim of the pelvis and in the right-occipito-anterior position. The membranes ruptured spontaneously 8½ hours after the onset of labour. Her pains were strong and occurred every 4 to 5 minutes but in spite of this the 1st stage lasted 23 hours the 2nd stage commencing at 4.30 in the afternoon of April 8th. After 12 hours of labour a vaginal examination revealed that the cervix was 3 fingers dilated, the foetal head in the right occipito anterior position and behind and to the right of the head there was a prolapsed arm. During the 2nd stage of labour, with the stronger pains, the patient experienced a cramp in the left gluteal region which was agonizing at times and caused her to scream. She could not lie on her left side for the delivery and was finally delivered in the dorsal position after a 2nd stage lasting just over 2 hours. The infant was a male weighing 9 pounds 10 ounces. The general condition of the infant was good and except for the development of oedema in the region of the right elbow joint which gradually subsided his neonatal period was uncomplicated.

On the first day of the puerperium the mother experienced 'pins and needles' in the toes and dorsum of the left foot up to the ankle. She said that she was unable to feel the nurse washing her foot, that the foot felt dead and she was unable to move it properly. On examination on the 4th day of the puerperium, it was found that the left foot was held in the position of equino-varus and that she could not dorsiflex the foot or toes. There

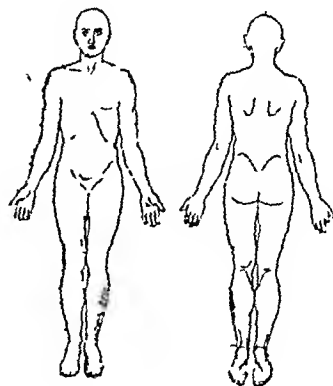
was some blunting of sensation to pin-prick over the lateral aspect of the left leg and over the dorsum of the left foot. A left sciatica nerve palsy predominantly affecting the common peroneal nerve, was diagnosed. The leg was supported by sandbags with the foot at a right angle. On the 11th

26 weeks after the delivery, there was no disability.

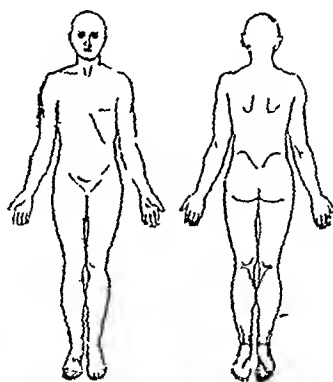
An X-ray pelvimetry, made after delivery, showed a conjugata vera of 4 1 inches and a transverse diameter of the inlet of 5 1 inches. The brim of this pelvis was slightly platypelloid.



Case 1



Case 2



Case 3

Diagram to show distribution of altered sensation to pin prick

day of the puerperium which was apyrexial, the patient was discharged with the left leg in a plaster-splint. The plaster encased the leg up to the knee and held the foot at right-angles to the leg. The toes were left uncovered on their dorsal aspect, and a walking iron was attached. The patient was encouraged to walk with the plaster and to attempt to dorsiflex the toes. The plaster was removed after 4 weeks when it was observed that she could dorsiflex the toes. When last seen

CASE 2 (G 421) Age 20, 1 para. This patient's previous pregnancy had resulted in an abortion at the 3rd month. The present pregnancy was uncomplicated, except that the foetal head was high and not engaging in the later weeks. The head could be pushed into the pelvis without any overlap at the 39th week of pregnancy. An X-ray pelvimetry at the 38th week of pregnancy showed a conjugata vera of 4 8 inches and the widest diameter of the inlet measured 4 9 inches. The

antero-posterior film of the pelvis and lumbar spine revealed (1) a scoliosis of the lumbar spine to the left (2) deformity of the pelvis due to some encroachment of the right side of the pelvis on to the pelvic cavity making the right oblique diameter larger than the left (3) apparent obliteration of the right sacro-iliac joint due to either a congenital deformity of the joint or an arthrodesis from a previous infective condition (4) normal appearance of the hip joints. The X-ray suggested a Naegele pelvis.

She was admitted in labour at term on August 16th 1941 at 7 p.m. She had started labour at 9 o'clock that morning. The foetus was presenting by the vertex which was above the brim and in the left occipito-anterior position. Her pains were weak at first and occurred every 10 to 20 minutes. The next day (August 17th) the pains were a little stronger occurring every 10 minutes and the head was engaging in the brim of the pelvis. On August 18th the head was engaged. The membranes ruptured spontaneously after 85 hours of labour. Following this the patient observed that her left leg felt somewhat useless and that she could not bear her weight on it. One hundred and four hours after the onset of labour a rectal examination was made and revealed that the cervix was fully dilated. Throughout the patient had been given sedatives liberally. Her general condition was good and the foetal heart rate was regular. The foetal head was seen high up in the vagina, $2\frac{3}{4}$ hours after the onset of the 2nd stage. Further advance of the head was not observed during the next 2 hours and it was decided to deliver the patient by the forceps. The foetal head was lying almost in the transverse diameter of the pelvis the occiput being in a plane slightly anterior to the sacrum and could not be manually rotated. Pelvic application of Milne Murray's axis-traction forceps was found to be impossible as the handles of the forceps could not be properly approximated. A cephalic application was then attempted. The left blade could be applied fairly easily but it was not possible owing to the shape of the pelvis to apply the right blade. Attempted cephalic application of Harg Ferguson's axis traction forceps was also unsuccessful. Keilland's forceps was then applied with some difficulty, but resistance to advance of the head seemed absolute on applying traction. Crani-

otomy was therefore decided upon. The skull was perforated and the dead foetus delivered by craniotomy forceps. The mother's condition at the end of the operation was quite good. The foetus was not weighed but appeared to be a good size.

On the 1st day of the puerperium the patient noticed a sensation of numbness over the lateral side of the left leg and beneath the arch of the left foot on the inner side. The left foot felt heavy and dropped easily. She did not complain of these symptoms however and was transferred on the 6th day of the puerperium to the base hospital where she remained until the 13th day. Her puerperium was apyrexial.

She attended the post-natal clinic 3 weeks after delivery and then complained, for the first time, of the numb sensation in the left leg and of the flapping foot. On examination it was found that there was weakness of dorsiflexion of the left foot and of abduction of the left thigh. There was some blunting of sensation to pin-prick over the lateral aspect of the left leg over the dorsum of the big toe and under the arch of the foot on the medial side. The ankle and knee jerks were normal. Paralysis of the left sciatic nerve predominantly affecting the common peroneal nerve was diagnosed. The patient was averse to having a splint and as there was some power of dorsiflexion of the foot she was treated by strapping the foot in a position at right-angles to the leg and instructed to wear low-heeled shoes. When this patient was last seen 22 weeks after delivery there was no disability to be detected on examination and she was free from symptoms.

CASE 3 (D 719) Age 26 1-para a blind congenital syphilitic patient whose Wassermann reaction was negative. Her previous pregnancy had resulted in the delivery of a live child weighing 8 pounds 9 ounces. Delivery was somewhat difficult and was effected with the aid of forceps. The present pregnancy was normal but in view of the obstetric history it was decided to admit this patient at the 39th week and induce labour. The foetal head at this time was free above the brim but could be pushed into the pelvis. X-ray pelvimetry showed a normally-shaped pelvis with a conjugata vera of 4.3 inches and the widest diameter of the brim measured 4.8 inches.

Surgical induction using a Jaque's bougie, was carried out at 10 a.m. on November 25th, 1941 after an unsuccessful drug induction on November 23rd. The vertex presentation was in the right occipito-posterior position. Twelve hours after the induction labour pains began. During the next 12 hours of labour the frequency of the pains increased but they were not strong; the foetal heart was regular at a rate of 140 to 148 per minute and the patient's general condition was good. The foetal head had not, however, engaged in the pelvic inlet. The bougie was removed from the vagina 15 hours after the onset of labour. The pains at this time were stronger and were occurring every 3 to 5 minutes. Twenty-four hours after the onset of labour, the foetal heart was not heard. The membranes ruptured spontaneously after 40 hours of labour. Three and a half hours later a vaginal examination was made and revealed that the split cervix was almost fully dilated in the transverse diameter owing to the split but was only 3 fingers dilated in the antero-posterior diameter. The vertex presentation was still in the right occipito-posterior position and the head was not engaged. As no further advance was made in the delivery during the next 17 hours and the temperature and pulse-rate had risen to 99.6 and 120 respectively, craniotomy was decided upon. Throughout the labour the patient was given sedatives liberally. Following the perforation of the head a large amount of cerebrospinal fluid escaped. The dead foetus was extracted with craniotomy forceps and a moderate pull. The foetus had a myelo meningocele and a small degree of hydrocephalus. It was not weighed but appeared to be of good size.

During the first few days of the puerperium which was apyrexial throughout the patient did not make any complaint of untoward symptoms. In view of our previous experience we asked the patient on the 3rd day whether her legs were quite well. She then told us that she had a feeling of 'pins and needles' in the right foot and had noticed that this foot did not feel as strong as the left but had not thought it worth mentioning.

On examination there was definite but slight weakness of the dorsiflexors of the toes and the ankle of the right foot. Other movements of the leg appeared normal. The ankle and knee jerks were normal. There was some hyperaesthesia to pin prick over an area which included the medial

four toes and the inner aspect of the foot, both on the dorsal and plantar surfaces. A right sciatic nerve palsy predominantly affecting the common peroneal nerve was diagnosed. The leg was supported by sand bags with the foot at a right angle. The next day the sensation of 'pins and needles' had disappeared. On the 5th day the sensation was normal but there was still some paresis of the dorsiflexors. On the 8th day of the puerperium she was allowed up and there was seen to be a tendency to drag the right foot. By the 10th day she was walking fairly well but very slight weakness of the dorsiflexors of the foot could be detected on examination. The patient was discharged on the 11th day with instructions to wear low heel shoes. This patient was seen 6 weeks after delivery and at that time had fully recovered.

DISCUSSION

Aetiology

Hunermann produced the first satisfactory explanation of the usual localization of the lesion. He attributed the predominant involvement of the common peroneal nerve to its position in the sacral plexus. He considered that the lumbo-sacral cord, as it passes over the ala of the sacrum, is injured by pressure, and that since this cord chiefly forms the main portion of the common peroneal nerve, the injury is manifest by paralysis of the muscles supplied by this nerve.

Thomas elaborated this explanation. He quotes Bardeen of Johns Hopkins University, who concluded, from his investigation of the sacral plexus, that the branches of the 4th and 5th lumbar nerves (lumbo-sacral cord), which go to make up the major part of the common peroneal nerve, are situated on the dorsal aspect of the plexus and therefore lie next to the bone of the sacral ala. Thomas suggests that these dorsal branches of the lumbo-sacral cord receive the chief injury as they lie on the bone and, therefore, the paralysis is chiefly localized to the distribution of the common

peroneal nerve. He adds that the gluteal muscles, which are also supplied by dorsal branches of the lumbo-sacral cord through the superior gluteal nerve, are not infrequently paralysed as well.

An abnormal increase in the intra-pelvic pressure is considered by Kleinberg⁸ to be the cause of a bilateral sciatic pressure neuritis and paralysis. He suggests that the fact that the pressure is not of the same intensity on all the nerves accounts for the peculiar and irregular distribution of the motor and sensory symptoms.

Pollock⁹ concluded that traumatic birth palsy of the peroneal nerve was due to trauma from the application of the forceps. He adds, however, that the lesion may occasionally occur, in cases of generally contracted pelvis, with difficult labour, as a result of pressure by the head of the foetus.

The pressure theory is criticized by Lambrinudi¹⁰. He states, "Were pressure the mechanism, one would expect the paralysis to occur on the side where the foetal occiput lay. In case 2 (which he reports in the article) the foetal position was left occiput-anterior but the paralysis was on the right side." He also points out that in a certain number of cases, towards the end of pregnancy, the patient complains of pains in the distribution of the sciatic nerve. "Pressure clearly cannot be responsible for the latter, for if the head has already sunk into the pelvis there can be no pressure, and if not there can be no pressure without active and painful contractions of the uterus." He quotes Brooks, who, from his study of pelves of patients who died shortly after labour, concluded that, during the 1st stage of labour, there was a rotation of the sacrum on the ilium in a backward direction, the axis being through the lower half of the auricular facet, and that the excursion in some cases was as much as a $\frac{1}{4}$ inch. Lambrinudi is of the opinion that

in a difficult labour this displacement would be even greater and that, as the lumbo-sacral cord is one of the tautest nerves in the body, this displacement would cause traction on the cord. "I would like to suggest, therefore," he says, "that the mechanism of this condition is that of traction on the lumbo-sacral cord, and that the lesion is probably located in the roots of this nerve rather than along its course. This theory would account for both the antepartum sciatic pains and the rare postpartum paralysis, for the loosening of the sacro-iliac joints, which permits the sacrum to rotate, occurs in the latter part of pregnancy."

Four cases of puerperal foot-drop, following forceps delivery, are recorded by Thomson, Harvey and Morgan¹¹. They attribute the paralysis "primarily to traction and torsion of the plexus, brought about by forcible rotation and traction of a mass firmly impacted in the bony pelvis."

Paralysis of branches of the sacral plexus may be caused by pelvic infection. Lloyd¹² quotes Hervieux, who, in 1870, reported a case of puerperal paralysis due to pelvic inflammation. Lloyd was of the opinion that, in the majority of cases of puerperal paralysis, septic infection was the cause. More recently, Lindén¹³ has reported a case of septic abortion with peritonitis, in which the patient developed a residual abscess and paralysis in the left leg localized to the common peroneal nerve. As the pelvic swelling subsided the paralysis improved. He writes, "I should not think it likely, however, that the paralysis was due to pure pressure effect. I should think it more likely that the inflammatory process has directly affected the nerve."

Trauma to the birth canal during labour predisposes the uterus and pelvic tissues to infection and so indirectly may produce a pelvic inflammation that can cause paraly-

sis A paralysis caused in this way might, therefore, be included under the heading of traumatic birth palsy. Such cases, however, are to be distinguished from those directly due to trauma by the presence of pelvic inflammation and the onset of the paralysis later in the puerperium.

The lumbo-sacral cord is derived from the anterior rami of the 4th and 5th lumbar nerves. It appears at the medial margin of the psoas major muscle and passes downwards and laterally over the pelvic brim anterior to the sacro-iliac joint. The dorsal part of the nerve is, therefore, in direct contact with the lateral part of the sacral ala as the nerve enters the true pelvis. Anterior to the nerve in this situation are the internal iliac vessels.

When the relation between the pelvis and the foetal head is such as to cause the head, or part of it, to lie over the lateral part of the ala of the sacrum, then there is no reason to believe that any pressure exerted by the foetal head would not deflect the internal iliac vessels laterally and directly press on the lumbo-sacral cord. The only structures then separating the foetal head from the nerve are the uterine wall, the peritoneum, extra-peritoneal fat and fascia. Such structures may possibly produce a cushioning effect for the anterior aspect of the nerve and this would tend to cause the brunt of the pressure to fall on the dorsal aspect of the nerve trunk, the fibres of which supply the common peroneal and gluteal nerves. With regard to the relation mentioned above, Tillman states, "The pelvis is so constructed that the posterior ilium is long, and its curve blends with the sacrum which curves backwards. The dimensions may be either generally contracted or there may be disproportion." Our experience, derived from these patients and from dissection of the cadaver, lends support to this view. It suggests that the part of the foetal head occupying the

posterior segment of the inlet of the pelvis may compress the lumbo-sacral cord in cases in which there is true disproportion or when, from some cause, the foetal head is deflected to one or other side of the pelvis. In such cases, the nerve is exposed to pressure provided that the part of the pelvic brim formed by the ala of the sacrum and the posterior half of the ilium has a gentle curve, concave anteriorly, and the promontory of the sacrum is not unduly prominent.

When one pole of the foetal head is in relation to the lumbo-sacral cord on one ala of the sacrum, it is extremely improbable that any other part of the head will have any direct relation to the other lumbo-sacral cord. The lesion will, therefore, be essentially a unilateral one except in certain circumstances to be mentioned later.

The pressure exerted by the head on the nerve is likely to occur at such time when the uterus is attempting to push the head into the pelvis, that is engaging, and when the head is actually engaged, for, as Linden points out, "if the small fontanelle is forced far down into the pelvis, the anterior part of the head becomes suspended at the inlet of the pelvis and exercises a continual pressure on the nerve trunks which increases at every pain." The pressure is likely to be greatest when the head is tightly fixed—and the uterine contractions are strongest. This will usually be when the 2nd stage of labour is being approached or has actually arrived. When the head is freely mobile above the brim of the pelvis, there is then no directing bony channel to keep the head in continuous contact with the nerve trunk. This provides an explanation for the time of onset of pain and other symptoms in the leg being during, and usually during the latter part of, labour.

Compression of a nerve produces interruption of its conductivity, which is usually

temporary and the severity of which varies directly with the force and the duration of the pressure. In general, the longer the duration of this compression, the less the force needed to produce a certain degree of interruption, and *vice versa*. During a delivery by the forceps, any pressure that may occur on the lumbo-sacral cord by the forceps themselves, would most probably take place during the actual periods when traction is made. The duration of such direct pressure by the forceps would be comparatively short. It is, therefore, improbable that the forceps directly can cause trauma to the nerve trunk so as to produce a severe palsy without a great deal of force being used with consequent injury to the maternal birth canal and other pelvic tissues. In our third patient, the nerve injury was considered to have occurred during the extraction of the foetal head by the craniotomy forceps. A moderately strong pull of short duration was needed to extract the incompletely collapsed head, the occiput of which was thought to have compressed the nerve trunk. This patient's palsy was of a very mild degree.

When traumatic paralysis follows delivery by the forceps, the injury to the nerves probably arises more commonly from pressure exerted by the foetal head, which is already active before the instrumentation and which is itself increased by the force exerted by the obstetrician through the forceps, when there has been little change in the obstetrical position of the head. Many of the reported cases mention the fact that the patients, who were delivered by the forceps, experienced pain in the leg during labour. Since the pain occurred before the application of the forceps, the primary pressure must have been from the foetal head and already active.

Bilateral traumatic paralysis, when it occurs, is probably to be explained, as

Lindén suggests, by the repeated application of the forceps in difficult labour when the position of the head is altered between the applications so as to affect first one side and then the other, or possibly in some cases by the foetal head affecting one side and the blade of the forceps, lying in the opposite diameter (with good cephalic application) affecting the other.

It is possible that the movement of the pelvis on the sacrum may cause a little traction on the lumbo-sacral cord and possibly contribute to a compression of the nerve as it passes over the sacral ala. If traction were the mechanism, as Lambri-nudi suggests, then there is no valid reason why the lesion should not be bilateral in all cases, for any movement of the pelvis on the sacrum is likely to be equal or almost equal to the two sacro-iliac joints. In our second patient the right sacro-iliac joint was obliterated. There is the possibility that a small amount of movement at the left sacro-iliac joint, which appears normal in the X-ray, might have occurred, but this must have been of very small extent with the stabilizing effect of the right arthrodosed joint. Lloyd drew attention to the fact that pressure on the sacral plexus can result from uterine and ovarian tumours in the non-pregnant patient and cause pain and paresis in the distribution of the plexus. He quotes a case of foot-drop and numbness in the leg caused by a large growth situated behind the uterus.

Sciatic pain in the later weeks of pregnancy would also be expected to be bilateral if movement of the pelvis on the sacrum were the cause. In any event, whether traction or pressure on the nerve trunk were the cause, such cause would reasonably be expected to be even more active during labour. Patients with sciatic pain in the later weeks of pregnancy would, therefore, be candidates for traumatic birth palsy. This has not been confirmed

by our experience and suggests that other factors are responsible for the pain in the majority of patients

CLINICAL PICTURE

During labour, which is usually prolonged and is often terminated by operative measures, the mother commonly experiences pain in the leg. This may be accompanied by spasmodic contractions of the leg muscles and severe cramp. The painful symptoms may be masked by analgesics and sedatives as Tillman has pointed out. Agonising cramp was experienced by the mother in the first case reported above, and prevented her from lying on her left side for her delivery.

The paresis or paralysis, depending on the degree of nerve damage, is present from the commencement of the puerperium and may be in evidence during labour itself. The 2nd patient was aware of a feeling of weakness of the leg during labour and it is possible that the liberal administration of sedatives masked any sensation of pain that may have been present.

Paraesthesia in the form of a dead feeling, or of pins and needles, is experienced early in the puerperium and often before the loss of motor power is appreciated by the patient. Hyperaesthesia, hypoaesthesia or complete sensory loss may be detected according to the severity of the nerve injury.

The nerves of the sacral plexus are those most commonly affected, and, of these, the common peroneal nerve suffers chiefly so that foot-drop is the common finding. The gluteal nerves are also frequently involved producing weakness of the gluteal muscles (Thomas, Stander¹⁴). Evidence of some injury to the tibial portion of the sciatic nerve may be found as well as the above (Lindén, Tillman). Pollock mentions that paralysis of the femoral

nerve has followed delivery of primigravidae on a number of occasions.

In the 3 patients reported here, the common peroneal nerve was predominantly affected. The gluteal nerves were also involved in the second patient. All 3 patients experienced paraesthesia, in 2 there was hypoaesthesia and in the third hyperaesthesia, chiefly in the distribution of the common peroneal nerve.

The deep tendon reflexes of the ankle and knee joints may be altered depending on the degree of sensor-motor disturbance and its distribution. The reflexes were unaltered in 2 of the 3 patients tested. There is no note of the reflexes of the third patient (Case 1).

The lesion is unilateral in the vast majority of the reported cases, and was so in the 3 cases described here, but bilateral lesions have been recorded on rare occasions. Thomas was the first to report a bilateral lesion.

There can be no doubt that these cases of traumatic birth palsy, when slight, may pass unnoticed. In our second case, the patient did not consider that the symptoms were worth mentioning until she found them persisting after discharge from hospital. The lesion in our third patient would undoubtedly have been missed altogether had it not been for our previous experience. Mild degrees of palsy may be seen and attributed to a functional cause. Salmond¹⁵ described 2 cases of puerperal paralysis which were considered to be of functional origin. Her second patient complained of severe pain in, and a feeling of weakness of, the left leg during labour. Movements of the leg were, however, observed during the labour. The patient had a long labour with an occipito-posterior position of the head. Manual rotation of the head was performed and a stillborn foetus delivered with the aid of the forceps. Numbness of the left leg was

experienced during the puerperium. She was allowed up on the 10th day of the puerperium, and it was found that she dragged the left leg behind her when she walked. Nothing abnormal was detected on examination of the nervous system at this time. She was treated for 10 days with massage and diathermy and was then discharged well. It is tempting to suggest, from the description of this case, that there was a mild degree of trauma to the sacral plexus during labour.

The possibility of a traumatic birth palsy occurring in the mother should be borne in mind in cases of 'trial labour' and notably in those patients who, during labour, complain of severe pain in one or other leg. Especially is this so if, in addition to the severe pain, there is evidence of spasmodic contractions of the muscles or paresis of the leg.

Traumatic paralysis in the distribution of the common peroneal nerve may occur during delivery from injury to the nerve as it winds round the neck of the fibula by external pressure. Such cases have been recorded by Morgan and Thomson.¹⁶ Traumatic paralysis produced in this way is not, however, peculiar to obstetrics, but its occurrence is worthy of note.

TREATMENT

Prevention of traumatic birth palsy occurring in the mother is extremely difficult. It is impossible to predict that a patient will acquire the lesion until she develops the warning symptoms of pain and cramps or paraesthesia in the leg during labour, but the possibility of its occurrence in a trial labour should be remembered. When the warning symptoms appear in a patient during labour, the danger of instrumentation should be borne in mind and delivery by Caesarean section considered if the child is normal and alive. Tillman suggests that "the multipara who presents a previous

history of difficult delivery, forceps delivery, stillbirth, recovery from nerve injury should have a Caesarean section." Such treatment will be prophylactic, not only for the birth palsy, but also for the occurrence of a dead baby.

The essentials of treatment of the established palsy are

(1) Careful splinting of the limb to prevent the occurrence of deformity and to hold the joints in such a position as to relax the affected muscles without, however, overlengthening the unaffected muscles. The splint should interfere as little as possible with the normal use of the unaffected muscles.

(2) To preserve the tone and nutrition of the muscles of the limb by encouraging voluntary, active movements of the limb. Such movements are more effective than massage and electrical stimulation, and are limited only so far as to prevent stretching the paralyzed muscles.

(3) To prevent stiffness of the immobilized joints by a daily period of passive joint movement being carried out.

PROGNOSIS

Tillman writes "These patients will all recover to some degree but many will remain paralyzed." But nerves supplying muscles of coarse and unskilled movements like the common peroneal and gluteal nerves tend to recover from injury more readily than those supplying muscles of fine movements such as the tibial nerve. Further, compression of a nerve usually produces a temporary, incomplete lesion of that nerve, with recovery of sensation preceding the return of motor power. These facts suggest that the milder cases of maternal birth palsy where the peroneal part of the sciatic nerve is affected should recover with proper treatment, and that, in the majority of such cases, the persistence of the dis-

bility is probably due to the overstretching of the paralysed muscles from the lack of early recognition and treatment of the lesion

Of the patients reported here, the lesion of the first was moderately severe, in the second it was mild and in the third very mild. All three patients have completely recovered from their disability

SUMMARY

(1) Three cases of traumatic birth palsy in the mother are described

(2) A brief review of the various suggested mechanisms by which the lesion is produced is given and the aetiology of the condition discussed. The lumbo-sacral cord (the anterior rami of the 4th and 5th lumbar nerves) is compressed, as it lies on the ala of the sacrum, by the foetal head when the relation between the pelvis and the foetal head is such as to cause the head, or part of it, to lie over the lateral part of the sacral ala, instruments by direct injury to the nerve may be responsible for the lesion in some cases

(3) The clinical picture is described. Attention is drawn to the warning symptoms of severe pain and cramps or paresis in the leg during labour. In such patients the danger of instrumentation is stressed and it is suggested that delivery by Caesarean section should be considered if the child is normal and alive. Especially is this so if the patient is having a trial labour

(4) The treatment of the established condition and the prognosis are briefly outlined. Early recognition and treatment of the lesion is an important factor in the prognosis

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The Lessons and Virtues of Salpingography

An Improved Technique

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DURING the last 17 years 2,000 cases of sterility in private and hospital practice have been investigated by Hystero-salpingography. As would be expected in such a large series not only has every known type of abnormal pathology been met with, but more important, often times one has been able "to search out the secrets of nature by way of experiment" as William Harvey commanded us.

The object of this communication is, however, not so much to demonstrate statistical findings, for these closely follow those of Samuel Meaker and have already been published, but rather to point out the lessons which can be learned and thereby popularize the art of salpingography, an art which hitherto has not earned in the profession the attention it deserves.

Undoubtedly there are pitfalls in the performance of salpingograms, and it may be these have deterred the busy or the timid from adventuring upon this new and scientific approach to the study of the complex problem of sterility, but apart from petty deterrents which are easily mastered, it is perhaps not yet sufficiently appreciated that the therapeutic results of hystero-salpingography are treble and even quadruply better than those of insufflation—a matter of considerable importance in these days of falling birth-rates.

In order to prove this, Dr E J Topham sent out a *questionnaire* to a large con-

secutive series of patients who had had salpingograms done by the author in the Sterility Clinic of Hammersmith Hospital. The replies, despite the fact that many letters came back undelivered from blitzed areas, showed that 31 per cent of the patients had conceived and gone to term. A similar follow-up of private cases done by the writer in conjunction with Dr S C Galstaun, Dr H W A Post, Dr G R M Cordner and Dr G T Calthrop, showed that 43 per cent had become pregnant.

Such therapeutic results may be due to the heavy poppy oil containing 40 per cent iodine acting bacteriostatically upon the mucous membrane of the uterus and Fallopian tubes, or possibly the lipiodol has a stimulative action upon the ciliary mucous membrane and the white tunic of the ovary, or peradventure it breaks down sticky adhesions and thereby reawakens rhythmic movement of the Fallopian tubes which once again can transmit an ovum from the fimbriae to the isthmus. Whatever the cause, if the oil be injected immediately after cessation of a period, conception frequently occurs within 3 months.

Then again, quite apart from its therapeutic value, one must recognize the superlative importance of salpingography in those cases in which doubt exists as to the ability of a woman to conceive after a septic labour or miscarriage, after criminal abortion, fulminant appendicitis, extra uterine

gestation and the like. Such problems frequently present themselves to the general practitioner and gynaecologist and may at times present a medico-legal aspect. An expert hystero-salpingogram will give the unbiased truth of what has chanced, and it is upon this evidence that the gynaecologist can give an opinion, and if need be plan the strategy and tactics of any surgical procedure.

Doubtless in the past many mistakes have been made retarding its popularity. Some have used too much oil, others have applied too much pressure, some have injected the oil under an anaesthetic in an upstairs theatre and then clumsily conveyed the patient with the apparatus *in situ* downstairs to an X-ray department, others unthinkingly have continued to use an instrument with a lateral hole for the conveyance of the oil with consequent exquisite cervical pain, and immediate spasm of both uterus and tubes, although it must be 12 years since it was pointed out that all pain could be obviated if the only hole was a distal one which allowed easy transit of the warmed viscous oil into the cavity of the uterus and tubes.

To-day the technique is simplicity itself and is only a matter of collaboration between radiologist and surgeon.

The patient who has previously been examined is asked to meet the gynaecologist in the hospital X-ray Department or the consulting room of the radiologist. She is placed upon the X-ray table in the dorsal position with the buttocks raised on a sand bag. One limb of a Barnes speculum being inserted the cervix is grasped by a vulsellum and painted with dettol or iodine. The nozzle of the syringe—whether it be the beautiful French instrument (as illustrated) which is straight and has a rubber cone, this is the one the author uses* or whether it be the curved and steel acorned

modification of Everard Williams—now being introduced and held taut against the cervix, the sand bag is removed. A fluoroscopic screen is then placed upon the abdomen and the lights are switched off. The warmed lipiodol or viscous neo hydriol is then injected and watched on the fluorescent screen passing from the uterus to the tubes and gently spilling (after 5 or 6 c.c. as a rule) into the peritoneal cavity. At the right moment, when a satisfactory picture is featured, the X-ray film is taken.

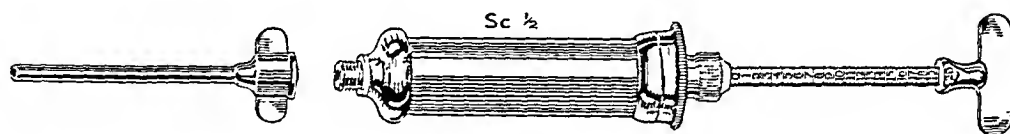
Anaesthetics are never necessary and are indeed better avoided. If the patient is nervous or one suspects from previous examination that she may be spasmophilic, by all means let her have $\frac{3}{4}$ hr. beforehand 1/100 gr. of atropine with, if need be, $\frac{1}{4}$ gr. morphia. In outpatients work where 6 or 7 patients are so examined one after the other neither of these injections is ever needed.

To give an idea of the mistakes committed in former times before the use of the fluoroscopic screen method, it may serve a useful purpose to observe Figs 1 and 2—the one showing extreme spasm of the uterus and an oil embolus in the uterine veins due to pressure, the other illustrating the mistaken use of 16 c.c. instead of 6 c.c. of lipiodol, even though the patient did later conceive and go to term. Oil embolus though somewhat alarming by reason of pallor and vomiting is only a temporary matter.

Figure 3 still more dramatically demonstrates the advantages of the new technique, for it shows how a careless operator can perforate the uterus. Fortunately this patient did not show any subsequent symptoms. Later she conceived and went to term.

On reviewing a large number of films and follow-ups, one appreciates where and why other mistakes are made. One of the commonest errors is to give a hopeless prognosis when the hystrogram shows that

* Made by Thackray of Leeds or Down Bros, costing £2 10s



C A



FIG 1



FIG 2



FIG 3



FIG 4



FIG 5



FIG 6



FIG 7



FIG 8



FIG 9



FIG 10



FIG 11



FIG 12



FIG 1



FIG 11



FIG 15



FIG 16



FIG 17



FIG 18



FIG 19



FIG 20



FIG 21



FIG 22



FIG 23



FIG 24



FIG 25

both cornua are rounded as in Figs 4 and 5. This happens most frequently when there has been a history of septic labour or criminal abortion. Long surgical experience of such cases, however, has demonstrated that with such a history there is only occlusion of the interstitial part of the tubes and that the distal portions are normally patent. For such, intrauterine tubal implantation can be done—successful results being in proportion to the improvement of the surgeon's technique. Bonney¹ has recorded 18 per cent success. I have had 2 patients out of 7 become pregnant and be delivered by Caesarean section, one other aborted at the 6th month. We must, therefore, admit that when (as the result perhaps of some former folly) a patient is willing to risk failure, that it is worth while performing this operation. Figs 6 and 7 are illustrations of the Fallopian tubes patent after tubo-uterine implantation by the method described by the author.²

Should, however, the history suggest gonorrhoea or acute salpingitis then it will be found that the Fallopian tubes are blocked just beyond the cornua and for their total length, vide Fig 8. In such, an operation was not worth consideration, but to-day such a statement needs qualification if the infection has been light and the treatment by sulphonamides has been concentrated, for quite a number of these patients are now being seen where the block is only at the fimbrial ends as in Fig 9.

In such, salpingostomy is worth while, for patency remains and pregnancy occurs. Should, however, one Fallopian tube be blocked or the occluded tubes be not distended at the distal ends, as in Figs 10 and 11, nothing will succeed. On the other hand if one tube is blocked and the other shows an oleo or hydrosalpinx, salpingostomy is worth performing. Figs 12 and 13 demonstrate such a case before and after operation (note the Michel clips still on the

wound). The patient conceived and had her baby 18 months later at Fulmer Chase Hospital for the Wives of Officers.

The use of amnioplastin will be found a great help in avoiding post-operative adhesions around the newly-opened tubal ostium.

One of the most important lessons to be learned by the gynaecologist is not to give a pessimistic prognosis or to say that the Fallopian tubes are occluded merely because (a) they cannot be seen in the film, or (b) they have a typical 'dog's ear' appearance at the cornua. This illusion is due to intense spasm of the sphincter muscles of the tubes at the cornua. Figs 14 and 15 are examples, and both these patients became pregnant within 3 months.

Sometimes when viewing the uterus through a fluoroscopic screen, or in a film, it is seen to be small and hypoplastic and the tubes appear to be long and tortuous—vide Figs 16 and 17. The inclination is to state that such a patient cannot become pregnant, but when one considers that conception can occur in the isthmial portion of a tube, such an argument based on size alone must be fallacious, for normal conception and nidation depends upon endocrine harmony.

Previous tubercular peritonitis or gangrenous appendicitis not only are a frequent cause of sterility, but also are responsible for mistakes being made in the interpretation of films. In such, oftentimes the uterus is retroverted and fixed by old adhesions and the Fallopian tubes if not occluded have a rosary or beaded appearance due to external kinks forming loculi as in Figs 18 and 19.

Contrary to expectation operative results are not always as happy as one might hope for in these cases. Fig 20 shows the end result of an operation done for retroversion and distal occlusion of the tubes subsequent to a gangrenous appendix and pelvic ab-

At first glance the film taken 6 weeks after operation gives the appearance of a perfect result, but if the control picture, Fig 21, taken 24 hours later is studied, it will be seen that the tubes have again become occluded at the distal ends, and thus despite the use of amnioplastin and perfect patency at the time of operation

Such disappointment, however, should not deter one for the evidence of years shows that more than 30 per cent of salpingostomies are successful

Every now and then the appearance of the uterus may cause surprise, for a filling defect due to an unsuspected sub-mucous fibroid may be seen which is directly or indirectly the cause of the sterility. Figs 22 and 23 are examples of this

Apart from morbid pathology it is necessary to draw final attention to the mistake of solely being guided by an antero-posterior picture when the uterus is retroverted or its size is in doubt. Oftentimes a very much better prognosis can be obtained by taking a lateral film which will, as in Figs 24 and 25 demonstrate not only the size and position of the uterus, but also the relation of the tube and its patency

Lastly it may be of interest and guidance to state categorically that during the whole period of these investigations using the technique described, never has there been a catastrophe or a case of infection

JOURNAL OF OBSTETRICS AND GYNAECOLOGY

I am greatly indebted to Dr G S Galstaun, Dr H W A Post, Dr E J Topham and Dr G T Calthrop for their untiring patience and help

Postscript

It must not be thought that every case of primary sterility is by any means routinely submitted to hystero-salpingography, for if there should be a history of dysmenorrhoea, or examination shows a high degree of flexion or displacement, they are admitted to hospital for dilatation and insufflation with or without shortening of the round ligaments

In some patients pregnancy has followed simple insufflation in the Outpatient Department or Consulting Room using without any anaesthetic Douay's Tubal Insufflation Instrument with a fine rubber acorned introducer in the cervix up to and above the level of the internal os. An assistant checks the dial reading by listening through the abdomen above the symphysis

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Simmonds's Disease

Due to Postpartum Necrosis of the Anterior Pituitary

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SIMMONDS'S disease is the syndrome which results from destruction of the anterior lobe of the pituitary. The destruction may be produced by various pathological processes. The most common of these is a gross necrosis of the anterior lobe which is caused by severe collapse of a parturient woman at delivery. The collapse is usually but not invariably a result of obstetric haemorrhage. In recent years the disease has gradually become better known clinically, but many cases still pass unrecognized. The chief difficulty arises from the fact that emaciation and premature senility, which are actually rather unusual concomitants, have unfortunately become accepted as the essential and basic characteristics of the disease. The real clinical picture of the disease has thus become somewhat obscured and mistaken diagnoses are made not infrequently. The following case of true Simmonds's disease, though only a single one, is described here for the precise reason that it is typical of the syndrome as it actually occurs, and not because it presents any unusual features. The patient had been under fairly continuous medical observation both at home and in various departments of 6 different hospitals from the onset of the disease, and

the diagnosis was finally proved by autopsy. The case was not investigated as completely as it would have been if the nature of the disease had been recognized during life. Nevertheless, the history is sufficiently full to illustrate most of the characteristic features of the syndrome.

Occurrence of the postpartum necrosis of the anterior pituitary

Before the sequence of events to be described, the patient was a normal healthy woman of cheerful character and active disposition. She married when she was 30 and, at the age of 32, she became pregnant of triplets. The pregnancy continued normally but the delivery was seriously complicated. The first baby presented as a breech and the body was delivered, but the head became locked with another head above the brim. She was admitted in this condition to hospital and, after considerable difficulty, was delivered of the first baby stillborn, and of two live babies. Soon after the delivery she became severely collapsed and was pulseless for several hours. Continuous intravenous and rectal salines were given, and coramine injected. The next day she was slightly improved, but still so ill that the

intravenous saline was continued up to 5 pints and the coramine repeated

This obstetric history is typical of the condition giving rise to anterior pituitary necrosis. The significant point is that she was severely collapsed after delivery and was pulseless for several hours. The diagnosis of a pituitary necrosis is presumptively justified on this fact alone. The only question which arises is the quantitative one—the extent of the lesion. If the necrosis is so large that the whole anterior lobe is virtually lost, the patient will inevitably develop subsequent symptoms of Simmonds's disease. If it is of medium size, she will escape the full syndrome but will show some indications of impaired pituitary function. If it is only a small necrosis, she will return to normal health. The prognosis at this stage may be assessed from the fact that, in general, the size of the necrosis is proportionate to the severity of the circulatory collapse suffered by the patient at the delivery. It should be noted that total or almost total loss of the anterior pituitary, either by postpartum necrosis or by operative removal as in the experimental animal, is not in itself fatal. The necrosis is only observed pathologically at this early stage if the patient dies of some other condition during the puerperium.

A key to the literature on postpartum necrosis is given by Sheehan,¹ but certain subsequent papers may be noted here. Plaut,² who was one of the early workers on the subject 20 years ago, has recently described a typical postpartum necrosis of the anterior pituitary in a woman who died two days after delivery, at which she lost about 1200 c.c. of blood and went into profound shock. Hutchison³ reports an interesting and unusual case in which a necrosis about 2 days old was found in the anterior pituitary of a woman 10 weeks pregnant. There was severe septic endometritis and pulmonary embolism which

had caused the patient to be very collapsed on admission 2 days before death, but the foetus was still *in utero*.

Progress during the puerperium

About 48 hours after delivery the patient was greatly improved and had a good pulse. No information is available about the condition of the breasts. Next day she developed puerperal septicaemia, with high fever and a leucocytosis of 27,000 per c.mm. The puerperal sepsis continued for several weeks during which she had various complications which are not relevant to the present matter. During this puerperal sepsis she lost a great deal of weight and much head-hair, but these were gradually regained during her prolonged convalescence in hospital. She was not discharged until nearly 5 months after the delivery. During her stay in hospital she had had 13 blood examinations. For the first month her erythrocyte count remained in the region of 3,200,000 per c.mm., and haemoglobin about 37 per cent. After this she was given much iron and there was a gradual and somewhat intermittent improvement so that, at discharge, her erythrocyte count was 4,300,000 per c.mm. and haemoglobin 60 per cent.

The puerperal sepsis was a result of the dystocia and is not to be considered as in any way a cause of the pituitary necrosis. Such sepsis is often quoted in textbooks as an aetiological factor in Simmonds's disease, in fact, as has been shown in previous articles, it does not usually develop until 2 or 3 days after the pituitary necrosis has occurred. The degree of anaemia in the early puerperium was about the same as that which usually accompanies puerperal sepsis (Crawford⁴). In the later puerperium the influence of the pituitary deficiency cannot be excluded as a factor in maintaining the anaemia.

Development of symptoms of Simmonds's disease

After the patient's discharge from hospital she was not really well. The weight that had been lost during the puerperal septicaemia had been almost completely regained though her face seemed rather thinner. She was remarkably pale, this was noticeable on her lips as well as her cheeks. She felt the cold extremely and, even in summer, spent the whole day crouching over the fire and complaining of the draught on so slight a pretext as a cupboard door being left open. She did not perspire any more. Her mental drive appeared to be lost and she was dull and somewhat reticent, but was still capable of an occasional quiet joking remark. She gave up her own house and went to live with her parents. She "couldn't be bothered" to do things and could not be persuaded to go out for walks or to visit her friends. Her appetite was very poor and there was some flatulence. She complained of a persistent physical weakness. And, a point of great importance, there was permanent absence of menstruation or of menstrual moulins from the time of the delivery.

In the course of the year after delivery she gained a few pounds in weight, and her face filled out to normal, but her other symptoms did not improve. Her medical attendant, 3 years after the delivery, noted that the pallor, the anorexia and the mental hebetude were the most prominent symptoms. Her speech was quite slow and she appeared to have slowness of apprehension in conversation. Her memory was poor, and in conversation she had to stop to think what she wanted to say. She had occasional attacks of slight stupor when she would refuse to answer questions. Her bodily strength was poor and her movements slow. Her hair was thin and very dry. Various medicines including iron and

liver extracts were tried without much benefit, though there seemed to be a definite subjective improvement when Radiostoleum was given for a few months.

The clinical picture as far as it goes is quite typical of true Simmonds's disease of this type—a pale woman of normal nutrition but with complete amenorrhoea, who sits all day close to the fire and has obvious slowing-down of her mental and physical processes, the entire condition dating from a delivery at which she was severely collapsed. It is clear at this stage that the pituitary necrosis must have been a large one.

First crisis

She continued in much the same condition until 4 years after the delivery. Then she had an acute illness of a very significant kind. One day she stayed in bed complaining of general malaise and a feeling of being chilled. She ate nothing at all on this day or the next 2 days, and became gradually rather more ill. Her bowels did not act at all. Late in the evening of the 3rd day she complained of dimness of vision and pains in the eyes. Within an hour or two she began to have a series of convulsions in which there was generalized twitching of the whole body and face. Between the convulsions she seemed confused and her speech was incoherent. She was admitted to hospital 2 hours after the beginning of the convulsions, in a semi-comatose condition with temperature 97°F, pulse-rate 76, and respiration-rate 20. By morning she was rather better but very lethargic, answering questions very slowly but fairly reasonably. She vomited small quantities of greenish fluid at frequent intervals. Her tongue was coated with white fur and her breath foul. There was lateral nystagmus in both eyes and the pupils were dilated. The systolic blood pressure was 90 mm Hg.

No other abnormality could be found on physical examination but this did not include the genital tract. She appeared to be very anaemic and her complexion was pink and white, but the blood was not examined. She was noted as being well nourished. Her Wassermann reaction was negative. The urine was normal on chemical and bacteriological examination and had a specific gravity of 1042. The next day her temperature rose to 104°F but, on treatment with M & B 693, it fell to normal on the day following. Radiological examination 2 days after admission showed some loss of translucency in the middle of the left lung, suggestive of inflammatory changes, this had disappeared a fortnight later. She was treated with iron, liver extracts and vitamin preparations and was said to be much improved on discharge from hospital 6 weeks after admission.

Crises of this type are quite characteristic of the later stages of Simmonds's disease and are the usual cause of death. The patients are always comatose, and convulsions and spasticity are common accompaniments. When a history can be obtained, it is nearly always found that the patient has eaten nothing for two or three days before the onset of the coma, this is due either to spontaneous anorexia or to vomiting or to some inter-current illness. The exact mechanism of the crisis is not yet quite clear. The blood sugar is extremely low in most of the reported cases, and the symptoms are very similar to those which occur in hypoglycaemic attacks in patients with islet tumours. Certain patients have been treated with intravenous glucose with apparent success. On the other hand, the picture is in some respects similar to an Addisonian crisis, as was suggested by Castleman and Hertz. At present all that can be said is that the crises are probably due to a complex of factors,

of which hypoglycaemia and adrenal insufficiency are the two most important. The rational treatment of the crises, according to this theory, should be the intravenous administration of large amounts of glucose and sodium chloride, combined with the administration of adrenal cortex extract.

Second crisis

There was a phase of temporary improvement after the first crisis, she set up her own house again a few months later and began to cook and do housework. Then she was involved in a motor accident and suffered a fracture of the left tibia about the middle of the shaft. The leg was put up in plaster in hospital and she was discharged a few days afterwards as a walking case. A week later, 9 months after the first attack of unconsciousness, she began to vomit green bile-stained fluid and felt very weak. After a day or two she became comatose and had convulsions. She was admitted to hospital in this condition. She soon regained consciousness and was quite rational, but her cerebration was very slow. There was a trace of albumin in the urine, and she appeared to be very anaemic, but the blood was not examined. Her reflexes were normal, and other abnormality was not found. She was given glucose saline by mouth and the bilious vomiting settled down. Within a week she was taking ordinary diet and seemed cheerful. Iron was prescribed and she was discharged in about 3 weeks.

She returned to live with her mother and attended as an out-patient at a hospital, where the plaster was removed 12 weeks after the fracture. The last X-ray report at 26 weeks after the fracture showed that union was not yet sound. Soon after this she was transferred to another department of the hospital, where a diagnosis of hypothyroidism was made on account of her

clinical condition and appearance. In addition, she was noted to be remarkably pale, so her blood was examined, unfortunately no details about this examination are now available, except that it did not reveal the severe anaemia that had been expected. For the next 4 months she was given an intensive course of thyroid, iron and liver extract but without any recognizable effect, so treatment was discontinued. During this time she gradually became depressed, dull and taciturn. She complained of frequent headaches and her speech became very much slower than before, but her weight remained about the same.

This second crisis was clearly a repetition of the first, and requires no further comment. The gradual development of indications of hypothyroidism in the last year is a common feature of the condition. As a result of this, many patients in the later stages of Simmonds's disease are diagnosed as myxoedema, but the diagnosis has to be reconsidered when it is found that they do not respond to treatment with thyroid. The pallor which was so consistently remarked upon in the present case is a frequent phenomenon, though some patients are described as sallow. Details of the blood examination in this phase are unfortunately lost, but there was only a trivial anaemia at the time of her final illness a few months later. It is possible that the pallor may, to some extent, be caused by narrowing of cutaneous vessels, an antithesis to the Cushing syndrome. A further explanation is suggested by the observation of Fraser and Smith⁶ that their Case 10, a Greek, lost his skin tan at the time he developed Simmonds's disease. The view that there may be some direct pituitary control of skin pigmentation also finds support in the fact that these patients never develop any Addisonian pigmentation despite the severe atrophy of the supra-renal cortex.

Third crisis and death

The patient died as a result of her third crisis 6 years after the delivery. One day, 14 months after the second crisis, she developed a complete loss of appetite and took only one cup of tea. She stayed in bed complaining of great exhaustion and was irritable when urged to eat. During the night she became nauseated, and vomited a little. The next day she was rather dazed but still refused to eat or to go into hospital. Early in the morning of the 3rd day she became delirious and semi-comatose, and within an hour or two she had a convulsion followed by deep coma. She was admitted in this condition to hospital, where she had several generalized clonic convulsions and remained unconscious. There was generalized spasticity most obvious in the legs, where adductor spasm was present, and the tendon reflexes were slightly overactive. The pupils were dilated, but ophthalmoscopic examination did not reveal anything abnormal. Her temperature was 96.4°F. Her pulse-rate was 80 per minute and her blood-pressure 70/50 mm Hg. Her respirations were only about 10 per minute. She was noted as being of stout build and well nourished and her muscles were normal. Blood count showed red-blood corpuscles 4,800,000 per c mm, white-blood corpuscles 6,000 per c mm, and haemoglobin 90 per cent. The heart, lungs and abdomen appeared normal, and lumbar puncture gave normal cerebro-spinal fluid. The urine was normal chemically and microscopically. During the day she had some sickness, for which she was given morphine and hyoscine, and glucose drinks. The next morning (i.e. on the 4th day), the coma deepened, her temperature rose to 101°F, her pulse-rate to 90 per minute, and she died.

POSTMORTEM FINDINGS

The skin showed a striking pallor which was very noticeable on the face. There was no axillary hair, a moderate amount of hair over the mons, and normal hair over the labia. The body appeared very well nourished on external examination, and had normal female contours. There was a full normal amount of fat in the subcutaneous tissues, the omentum and round the heart. The *pituitary* was very small, particularly the anterior lobe, which was shrunken and peculiarly translucent. The weight of the whole gland, including a considerable amount of fat and connective tissue from the sides of the lateral sinuses, was 0.42 gm, which is about half the normal. Microscopically the anterior lobe consisted almost entirely of loose fibrillar connective tissue enclosed in a much thickened fibrous capsule. Small groups of apparently healthy anterior lobe cells were present in certain places, (a) the largest mass, about 20 acini in horizontal sections, lay at the upper part of the "middle lobe" just beneath the stalk, (b) several very small islets, each about 2 or 3 acini in section, were embedded at various points at the sides in the deeper parts of the thickened capsule. These groups of remaining parenchyma were not fibrosed at all, but there was some formation of small colloid cysts in them, particularly in the sub-capsular islets. The posterior lobe was smaller than usual. It showed an obvious decrease in the amount of fibrillary material relative to nuclei, and had two small lymphocyte aggregations near the middle lobe and slight infiltration of the usual wandering basophiles in front. The *adrenals* were very small and thin. Their combined weight, without dissecting off the not inconsiderable amount of fat and connective tissue which adhered to them, was 3.5 gm, as compared with a normal

of 10 or 12 gm. The cortex was extremely thin and could scarcely be distinguished from the medulla with the naked eye. The *thyroid* was brown and very small, weighing 8 gm as compared with a normal of 20 or 30 gm. Microscopically it showed an extreme atrophy like that in myxoedema. About half of the gland consisted of masses of lymphoid cells, often arranged in follicles with very large germinal centres. The remaining alveoli were of two types: small alveoli of about 30 μ diameter with flat epithelium and full of deeply eosinophile colloid, and rather smaller alveoli with cubical epithelium and practically no lumen or colloid. There was a relative excess of fibrous tissue throughout. The *ovaries* were like those of an old woman. Microscopically there were a few old corpora albicantia, and two small and atrophic Graafian follicles were found. The *uterus* was very small. Its walls were 6 mm in thickness, which is about half the normal for a patient of this age. The endometrium was reduced to a single layer of cubical epithelium lying directly on the muscle, with a complete absence of sub-mucous stroma. Occasional very small cysts lined by cubical epithelium were present immediately beneath the surface epithelium, representing the remnants of endometrial glands. The muscle fibres showed a very considerable loss of their cytoplasm only, so that sections of the myometrium showed numerous bundles made up almost entirely of smooth muscle nuclei and separated from neighbouring bundles by an excess of fibrous tissue. The cellularity of the bundles approached to that of a sarcoma. The *kidneys* weighed 64 gm each, the normal being about 150 gm. They showed atrophy of cortex, medulla and pelvis equally, so that they might have been taken for a child's kidneys. The thickness of the cortex was 3 mm, which is about half the normal

The glomeruli and tubules were small but normal apart from the presence of an occasional hyalinized tuft. The *heart* weighed 190 grm as compared with a normal of 260 grm. It showed some atrophy of myocardial fibres with slight excess of lipofuscin and very occasional small foci of lymphocytic infiltration. The *liver* weighed 1150 grm, the normal being about 1500 grm. It was microscopically normal. The *pancreas* was small but did not show any histological abnormality of acini or islets. The *stomach* had numerous masses of lymphoid tissue in the deeper mucosa. The mucosa at the pyloric end appeared otherwise normal, but the mucosa at the cardiac end had the same histological structure as that near the pylorus. The *mammæ* were normal on external appearance, but no breast tissue at all could be found in three blocks taken beneath the nipple. The *spleen* was normal macroscopically and microscopically. Haemosiderin was not found in any of the viscera. No abnormality was noted in other organs apart from moderate oedema of the lungs.

These pathological findings are quite characteristic. The original necrosis of the anterior pituitary was a very large one but had spared, as it usually does, a small area just beneath the stalk and a few islets of cells beneath the capsule. After a period of secondary atrophy at its margins, the necrosed area gradually became absorbed, leaving only its condensed fibrous framework. The small remnants of the anterior lobe spared by the necrosis persist at the surface of the shrivelled scar. They represent scarcely 1 per cent of the original lobe and, from a physiological aspect, their function would be insignificant in amount. The extreme atrophy of the suprarenal cortex and of the thyroid are the result of the pituitary insufficiency. The atrophy of the ovary, most obvious histologically, is due to the same cause, and the atrophy of

the uterus is secondary to the ovarian dysfunction. The peculiar type of atrophy of the myometrium is presumably to be related to superinvolution occurring in a gravid uterus. The reduction of the endometrium to a single layer of epithelium explains why endometrial biopsy is always unsuccessful in these cases (McLellan, Fraser and Smith). Other quite standard findings are the loss of body hair, the good state of general nutrition of the body, and the small size of certain viscera. In this case, the splanchnomicria involved the kidneys to a very marked degree.

DISCUSSION

Patients' with fully developed Simmonds's disease of this type often present something of a diagnostic puzzle. Their illness dates from a delivery at which they have been severely collapsed. Afterwards they appear to be suffering from a puerperal debility from which they never convalesce properly, and which is obviously something much more than mere "debility." They have permanent amenorrhoea. They may have little appetite, but usually do not become thin. They are sometimes very pale but blood counts do not show an anaemia severe enough to account for the pallor, and treatment with iron or liver extracts has little or no effect. They have evidence pointing to mild or even severe myxoedema, but they do not improve on treatment with thyroid. Their condition can suggest Addison's disease, but does not show any pigmentation. They are subject to occasional attacks of coma, which are not due to any of the usual causes of coma in general, and which often prove fatal. The general clinical picture thus drawn may seem disappointingly indefinite. There are, however, a number of positive physical signs which, if taken

together, will establish the diagnosis conclusively. There is superinvolution of the uterus, vagina and vulva, a loss of the axillary hair and a thinning or loss of the pubic hair. The superinvolution, and possibly the body hair loss also, may be taken as evidence of loss of ovarian function. The basal metabolic rate is about -30 which is presumably an indication of loss of thyroid function. There is a disappearance of 17 ketosteroids from the urine, indicating loss of function of the adrenal cortex. The insulin tolerance test shows a hypoglycaemia unresponsiveness which results from the deficiency of adrenal cortical hormone, and an insulin sensitivity due to the lack of glycotropic hormone from the pituitary. These last two very important tests have only recently been introduced by Fraser and Smith. The detailed application of the tests to Simmonds's disease is given in their paper, the more general aspects were dealt with by Fraser, Forbes, Albright, Sulkowitch and Reifenstein⁸ and by Fraser, Albright and Smith.⁹ When there is evidence of simultaneous loss of function of gonads, thyroid and adrenal cortex, combined with the lack of pituitary glycotropic hormone, the diagnosis of very gross loss of function of the anterior pituitary is established beyond reasonable doubt.

This description is based essentially on the facts given in recent reviews (Sheehan¹⁰ and ¹¹) of the previous literature on Simmonds's disease of this type, with details of the 37 cases with autopsy that had been published at that time. Certain further papers require consideration. Fraser and Smith have recently published an important paper dealing with the 2 objective tests mentioned earlier. In this paper they give full details of 10 patients with anterior pituitary deficiency, of which the first 4 are quite typical Simmonds's disease due to postpartum necrosis of the anterior pitui-

tary. These 4 patients are still alive but the clinical evidence is quite conclusive. Means, Hertz and Lerman,¹¹ in a paper stressing the hypothyroid aspects of Simmonds's disease record 6 cases of the present type. Their Cases 2 and 7 dated from a delivery about which information is not given, but the autopsy findings were characteristic. Their Cases 3, 4, 5 and 6 followed postpartum haemorrhage, and postmortem proof was obtained in the last 2 of these. Further details about their Case 2 are given by Castleman and Hertz, their Cases 3 and 4 are also described as Cases 1 and 2 by Fraser and Smith. Their Case 3 is also described as Case 1 by Lerman and Stebbins¹² who record also an additional case which followed postpartum haemorrhage and was proved by autopsy 40 years later. Biggart¹³ records 2 cases, in one of which there had been retained placenta and, in the other, some unknown severe obstetric complication. Both were proved by autopsy. Biggart also illustrates 2 pituitaries with postpartum necroses, 1 a week old and the other 2 years old. Pettersson¹⁴ records a case with typical obstetric and clinical history, the autopsy findings were characteristic and the pituitary was very small but it was not examined microscopically. Seeger¹⁵ describes a case with autopsy findings and clinical history which are compatible with the diagnosis though the obstetric history is not recorded. Schob and Guntz¹⁶ report a case with acceptable autopsy findings but an indefinite obstetric history, this patient was strikingly emaciated. Cases with very characteristic obstetric and clinical histories but without autopsy are recorded by Stenstrom,¹⁷ Adler,¹⁸ van Rijsewijk,¹⁹ de Langen²⁰ (Case 1), van Balen,²¹ and Williams and Whittenberger²² (Case 1). Possible clinical cases are also noted by Karrenberg,²³ Loos,²⁴ and Mogensen²⁵ (Case 3). An article by Vignes²⁶ on the subject is not at

present available Escamilla and Lissner² review the literature on Simmonds's disease and anorexia, and give a very extensive bibliography (They had published a short abstract of their main findings earlier³) From a personal study of the original case reports it appears that some of the cases they review can be accepted as true and uncomplicated cases of Simmonds's disease, some are grossly complicated by neoplasms which involved the hypothalamus, whilst in the rest, a large percentage of the total, there is nothing to suggest that any pituitary lesion had occurred Their conclusions are thus not to be accepted without a very critical analysis of the actual cases on which their review is based

The best line of treatment of these cases is still not fully worked out The production of a subsequent pregnancy leads to definite clinical improvement (Sheehan and Murdoch³⁹) Endocrine substitution therapy has recently given some very promising results in the hands of Williams and Whittenberger and of Lerman and Stebbins There is also some indication that the crises may be avoided by keeping the patient on a high salt diet and by insisting that she shall never go a single day without adequate food intake

SUMMARY

A case is reported of Simmonds's disease due to postpartum necrosis of the anterior pituitary The clinical course was quite typical and, as is usual in these cases, the patient remained well nourished She died 6 years after the delivery At autopsy all the characteristic changes were found

The recent literature on the subject is reviewed, bringing the total cases proved by autopsy up to 48

Our thanks are due to Professor J Shaw Dunn for his encouragement and advice, and to the following who have kindly

supplied the clinical details from which the history of this case was gradually pieced together Drs Douglas Adams, Western Infirmary, Glasgow, and Stobhill Hospital, Glasgow, P M Birks, Gloucestershire Royal Infirmary, W G Birks, Gloucester City General Hospital, G Browning, Western Infirmary, Glasgow, A S Glover, Glasgow, C Latto, Prince of Wales Hospital, Plymouth, D Latto, Herefordshire General Hospital, W A MacLennan, Western Infirmary, Glasgow

One of us (N G B McL) is indebted to the Rankin Fund of the University of Glasgow for a grant in aid of histological expenses

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Accurate Pelvimetry*

BY

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INTRODUCTION

THE function of pelvimetry by X-rays in the prognosis of labour is not yet appreciated as it should be either by obstetricians or by radiologists. In the use of this diagnostic procedure it is so easy to forget that difficulty in labour, which can properly be attributed to disproportion, is a comparatively rare mischance in obstetric practice.

Now disproportion is a word that is far too loosely used in writings on obstetrics, but if we limit its use to cases in which the expulsion of a fully-flexed foetal head is obstructed by a narrowing of the bony canal of the pelvis at any level we can be certain that disproportion causes difficulty in considerably less than 5 per cent of all labours. The first function then of pelvimetry by X-rays is to diagnose early in pregnancy, or even before marriage, that 5 per cent of patients in whom difficulty may occur so that the labour may be arranged under the best conditions, and so that the remaining 95 per cent may be assured that their confinements are to be free from that one danger at any rate. The recognition of this unfortunate 5 per cent is an exercise in the calculus of probability which can be solved by a statistical appreciation of the variation of the maternal pelvis and the foetal skull and this can only be obtained from a considerable series of accurate measurements. To say, as some writers do, that pelvimetry without cephalometry is valueless is a council of ignorance. The second function of pelvimetry is to assist

the obstetrician in making up his mind as to how far he is justified in interfering with the normal course of labour, here cephalometry is essential. In this regard it must constantly be emphasized that a disproportion which is not absolute is only one of many factors which influence the decision, that of two women with a similar degree of disproportion, one may safely deliver herself while the other may require a Caesarean section. Here again a sound opinion must be based on accurate measurements and a statistical view of previous experience and should never be given except in terms of probability, the dictum that pelvimetry by X-rays has made trial labour an improper procedure is certainly not yet justified if it ever will be. Now there is some legitimate doubt as to whether measurement by X-rays is indeed sufficiently accurate for these two purposes, and this paper is an examination of the degree of accuracy which can be obtained by one technique of measurement at any rate. It will be well to give that technique in some detail so that it may be fully appreciated that the statistical method which is used to determine the probable error is really applicable.

THEORY OF THE TECHNIQUE

The technique is a stereometric one, that is it depends on the use of two exposures, it is similar in many respects to that of Hodges¹. The theory makes use of three simple geometrical propositions which are

* This research is assisted by a grant from the Medical Research Council

almost self-evident from a consideration of Plate I. The tube with its focus at T is at a height TP above the film, the line TP representing the normal ray, an object at A will then cast a shadow on the film at S, if the tube is now moved parallel to the film to a position T' the normal ray is T'P' and A casts a shadow at S', SP and S'P' are joined to intersect at N. Then —

(1) SS' is parallel to PP' which is parallel to TT'

(2) AN is perpendicular to the film, i.e., N is the projection of A on the film

(3) $AN = TP \times SS' - (SS' + PP')$

The proof of these propositions is given in Appendix I

Now it is evident that if this construction were made for all points of a solid object like the pelvis the result would be a right projection of the object on the film, such as would be produced if the tube were at an infinite height above the film, with this addition that the height of any point in the object above the film can be accurately ascertained if the focus-film distance, TP, and the tube-shift, PP', are known and if the shadow-shift, SS', is measured. It might be well to state here that I use a focus-film distance of 80 cms, and a tube-shift of 10 cms. Applying this to pelvimetry it is obvious that the length of any diameter is the length of its projection on the film provided that its terminals are at the same height above the film, if they are at different heights this will be recognized by a difference in their shadow-shifts, and the length of the diameter will be the hypotenuse of a right-angled triangle the other sides of which are (1) the length of the projection on the film and (2) the difference of height of the two terminals. This theory is, of course, not limited to pelvimetry, it forms the basis of a method for the rapid location of foreign bodies, and it could be used for any anatomical measurement.

APPLICATION OF THE THEORY

I have² published my opinion that five measurements only are necessary for the prognosis of labour, (1) The obstetric conjugate, and (2) the transverse diameter at the brim, these give the area of the opening at the brim, (3) the diameter between the ischial spines and (4) the pubosacro-coccygeal diameter which give the area at the plane of least pelvic diameter, (5) the subpubic angle. I have shown, and my findings have been confirmed by Ince and Young³ that the use of the forceps in labour is more closely associated with contraction of this angle than with any other measurement of the pelvis, and it seems clear that a system of pelvimetry is not complete which fails to give an accurate value for the pubic angle. The first three measurements may be made from the usual films taken with the brim roughly parallel to the film, and the last two may be made from films taken with the brim roughly at right angles to the film. The layout for these two positions is shown in Plates II and III, as it is not necessary with this technique to stress accuracy of positioning, attention has been concentrated rather on rapidity and ease of positioning. The Bucky diaphragm is supported at an angle of 35° to the horizontal which corresponds to the angle of average tilt of the pelvis, so that with the patient recumbent and with the buttocks closely apposed to the diaphragm the first position is reached, for the second the patient abducts the thighs, sits up, and leans as far forward as possible. Both positions are easy to secure and to maintain, and undressing beyond the removal of metal parts of the clothing is not required. The resulting films are shown in Plates IV and V, and it can be seen that these two positions will give shadows of the foetal head from which measurements of the biparietal and suboccipito-bregmatic

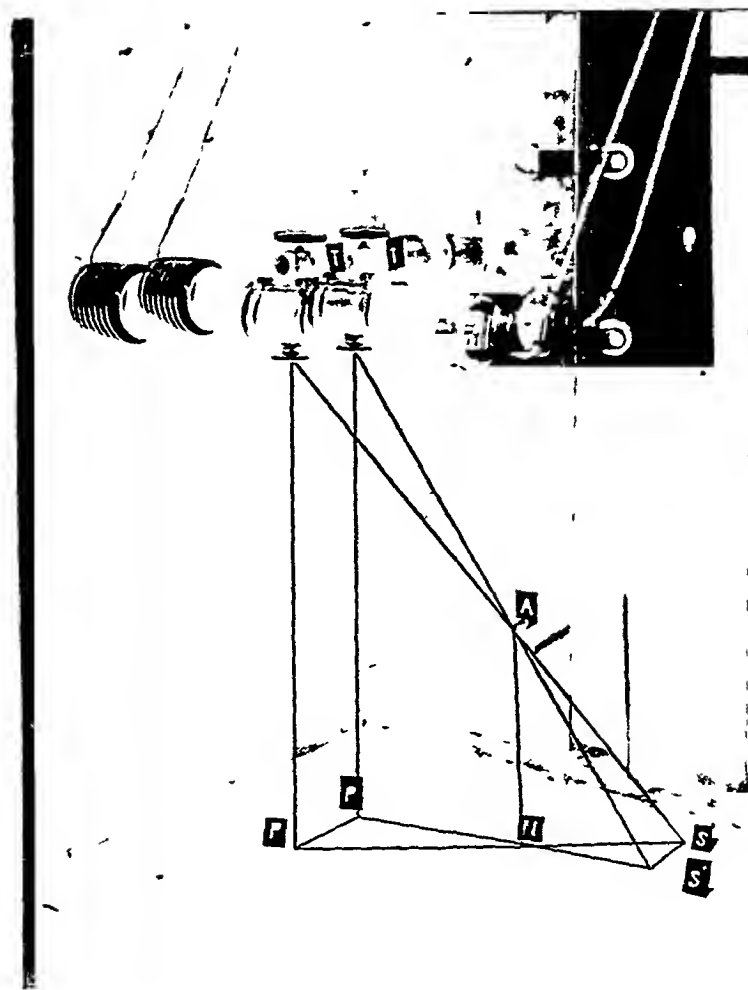


PLATE I
The geometry of stereometric measurement



PLATE II

It is out for radiography of the hind of the pelvis

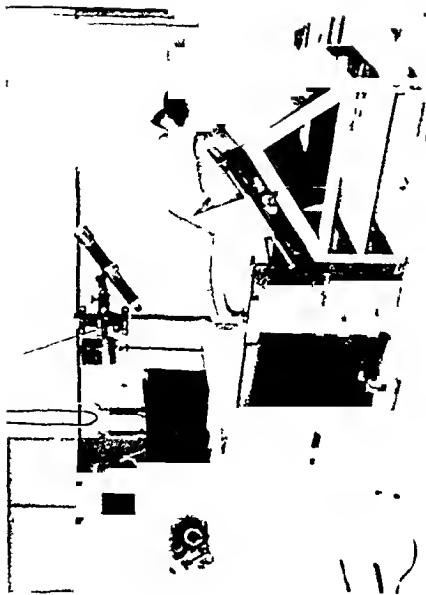


PLATE III

It is out for radiography of the outlet of the pelvis



PLATE IV

Radiograph of the hind



PLATE V

Radiograph of the outlet

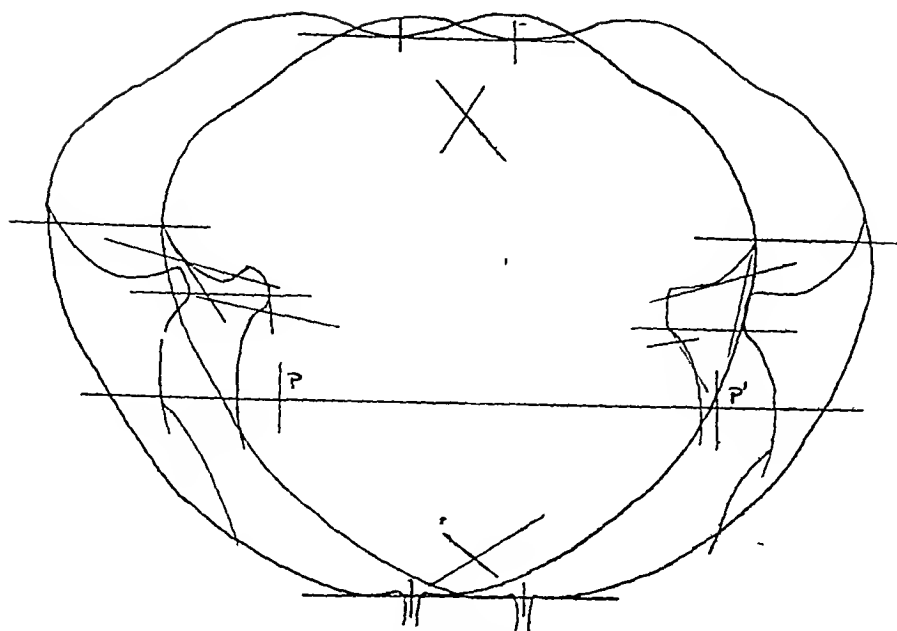
diameters may be accurately made. Small lead markers are inset in the centre line of the diaphragm at a distance of 5 cms from the centre (these are shown clearly in Plates IV and V), and the tube is centred so that at the limits of shift, the normal ray passes through these points, marks on the tube-stand, cross-arm, and stub make it easy to repeat this centring at will. It is possible, but rather confusing, to make both exposures on one film, in practice two films are exposed in each position and these are marked left and right during exposure.

The right film is set up on the viewing box with a piece of tracing paper so that the edge of a T-square passes through the shadows of the lead markers, a line is drawn through these and the left-hand shadow is marked P, a point on the line 10 cms to the right is marked P'. The outline of the pelvis is drawn and the terminals of the required diameters marked, through these points lines are drawn parallel to the tube-shift by means of the T-square. The tracing is now superimposed similarly on the left film so that the point P' coincides with the shadow of the right-hand marker and the line PP' passes through the other shadow. The parallel lines now pass through the shadows of the same points on the left film and these are marked, the intersecting lines, SP and S'P', are ruled and the projection is complete, the projections of the diameters may now be measured. Examples are given in Plates VI and VII. The shadow shifts are measured and any difference in height of the terminals is calculated, and the diameter corrected accordingly. It should be noted that the arithmetical work can be rendered unnecessary by the use of a table for the height and a nomogram for the calculation of the hypotenuse. For all the diameters except the pubo-sacral this correction is rarely necessary as the difference

in height must exceed 10 mm before it need be taken into account, it is never necessary in the case of the pubic angle.

THE PROBABLE ERROR OF OBSERVATION

Measurements made by this technique, which has now been used in over 600 cases, are stated to the nearest millimetre, this unit of measurement is very necessary for statistical work and it is essential to discover how far the claim to this degree of accuracy is justified. Chassar Moir⁴ expresses his doubt in these terms "some methods (such as that of Dr Nicholson in this country and the recently described methods of Hodges of Chicago) aim at high accuracy," and this legitimate scepticism must be satisfied, it must be shown that the method not only aims at, but achieves high accuracy. The first source of error would be in the setting up of the tube, couch, and diaphragm, because the technique does undoubtedly depend on the accuracy of the two constants, the focus-film distance and the tube-shift. Now it is not very difficult to prove mathematically that any error of a magnitude which is likely to occur in these constants would have an effect of the order of 0.1 mm on the measurement of any diameter, so that we may legitimately dismiss this source of error. Faulty positioning of the patient, like poor quality of the films taken, will have the effect of making the films more difficult to read but has no real effect on the accuracy. The main source of error without doubt lies in the interpretation of the films, the recognition of the terminals of the diameters, and in the use of draughtman's tools and scales. This error is purely a personal one, and any observer is just as likely to make a measurement too large as too small, the error is indeed a true error of observation and should conform to the mathematics of the error.



PLAT. VI
Stereometric tracings of the brim

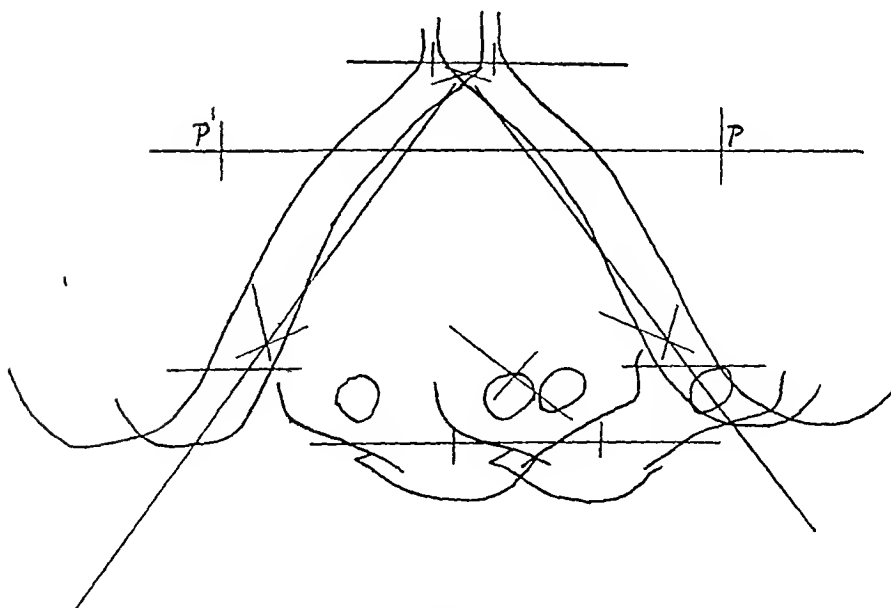


PLATE VII
Stereometric tracings of the outlet

function That being so it permits the use of an interesting statistical technique to determine the amount of the probable error of any two observers, the theory of the technique is given in Appendix II It is obvious that the two observers must make their measurements quite independently of each other In my case the second observer has been a secretary, Miss B, who, while of more than average intelligence, was quite ignorant of anatomy and quite unskilled in the use of draughtsman's tools After a period of instruction in the technique lasting a few weeks, Miss B was asked to measure 30 sets of films and to tabulate her results without referring to the results which I had previously obtained From these measurements the probable error of both observers was calculated as in the table below

	Probable Error of Accuracy	
	N	Miss B
Conjugate (mm)	0.24	1.04
Transverse (mm)	0.65	0.95
Ischial spines (mm)	1.30	2.96
Pubo sacral (mm)	1.66	3.68
Pubic angle (degrees)	1.04	1.05

"Probable Error" has, of course, a precise significance, one half of the observations are likely to have an error less than the probable error, the errors in the other half are likely to exceed it, and an error of thrice the probable error is not likely to occur oftener than twice in 100 measurements It is now possible to say that the claim to give measurements of the diameters to the nearest millimetre is, on the whole, justified Further it appears that knowledge of the anatomy of the pelvis and a familiarity with the technique for 10 years give less advantage in accuracy than might be expected Skill in the technique, however difficult it may seem at first sight, can be acquired in a very short time indeed

CONCLUSION

Scientific research in any subject has only two lines of approach, (1) the accumulation and examination of statistical material, and (2) the carrying out of a planned experiment, for both these purposes accurate measurement and biometric methods are absolutely essential This truism must come to be accepted in the ward as it is already universally accepted in the laboratory In this respect research into the value of pelvimetry by X-rays in the prognosis of labour is in a lamentable state Greulich and Thoms⁷ have accumulated a great deal of material which is shorn of most of its value for lack of biometrical examination Caldwell and Moloy⁸ have tried to relate difficulty in labour to the shape of the pelvis, but their classification of the pelvis depends on purely subjective impressions and accurate measurement is simply not used Chassar Moir uses a full scale outline of the brim and outlet of the pelvis on which he superimposes an outline of the foetal head, but here again his judgment as to the course of labour is purely subjective and appears to take little account of alteration of shape of both foetal head and maternal pelvis under stress O'Sullivan⁹ confines himself to a comparison of the conjugate and biparietal diameters from which he assesses the need for Caesarean section

There is no hope of progress on any of these lines, indeed there is little hope of progress until we have obstetricians who will have the courage, the vision, and the patience to make an extensive use of trial labour combined with biometrics and accurate measurement

APPENDIX I

TP is perpendicular to the plane of the film so that the plane in which the triangle, TPS, lies is perpendicular to the plane of the film, similarly the plane in which the

triangle, TP'S', lies is also perpendicular to the plane of the film, therefore AN, the intersection of these planes, is perpendicular to the plane of the film

TP and AN are both perpendicular to PS so that the triangles SAN and STP are similar, and

$$\begin{aligned} & \text{SN SP AN TP,} \\ & \text{similarly S'N S'P' AN T'P',} \\ & \text{but TP=T'P',} \end{aligned}$$

therefore SN SP S'N S'P', and the triangles SNS' and PNP' are similar, and SS' is parallel to PP'

Again in the similar triangles SAN and STP

$$\begin{aligned} & \text{AN TP SN SP} \\ & \text{SN (SN+NP),} \end{aligned}$$

and in the similar triangles SNS' and PNP'

$$\text{SN NP SS' PP',}$$

therefore

$$\text{SN (SN+NP) SS' (SS'+PP'),}$$

$$\text{and AN TP SS' (SS'+PP'),}$$

$$\text{so that AN=TP} \times \text{SS' - (SS'+PP')}$$

APPENDIX II

Any value, D, of a variable such as a diameter of the pelvis may be written as $\bar{D}+d$, where \bar{D} is a constant, the mean, and where d is the deviate from that mean, if a number N, of observations is made then $\Sigma d=0$, and $\Sigma d^2/N=\sigma_d^2$, i.e. the square of the standard deviation. If now an observer makes a number of measurements of D, any value which he gets, A, may be written as $\bar{A}+d+\alpha$, where \bar{A} is the mean of his observations, d is the true deviation from \bar{D} as before, and α is an added deviation arising from his error of observation. If this observer makes N measurements and these are squared and summed

$$\begin{aligned} \Sigma A^2 &= \Sigma [\bar{A}^2 + 2\bar{A}(d+\alpha) + d^2 + \alpha^2 + 2d\alpha] \\ &= N\bar{A}^2 + \Sigma d^2 + \Sigma \alpha^2 + 2\Sigma d\alpha \end{aligned}$$

$$\text{and } \Sigma A^2/N = \bar{A}^2 + \sigma_d^2 + \sigma_\alpha^2 + 2r_{d\alpha}\sigma_d\sigma_\alpha$$

but his error of observation is independent of the variation of the true measurement D, and this is true even if the absolute magnitude of α tends to vary with the absolute magnitude of d, so that $r_{d\alpha}=0$, and

$$\Sigma A^2/N = \bar{A}^2 + \sigma_d^2 + \sigma_\alpha^2$$

For the same series of observations by a second observer

$$\Sigma B^2/N = \bar{B}^2 + \sigma_d^2 + \sigma_\beta^2$$

If we now sum AB we have

$$\begin{aligned} \Sigma AB &= N\bar{A}\bar{B} + \bar{A}\Sigma(d+\beta) + \bar{B}\Sigma(d+\alpha) \\ &+ \Sigma d^2 + \Sigma d\alpha + \Sigma d\beta + \Sigma \alpha\beta \\ &= N\bar{A}\bar{B} + \Sigma d^2 + \Sigma \alpha\beta \end{aligned}$$

$$\text{and } \Sigma AB/N = \bar{A}\bar{B} + \sigma_d^2 + r_{\alpha\beta}\sigma_\alpha\sigma_\beta$$

but the errors of the two observers are purely personal and must be independent so that $r_{\alpha\beta}=0$, and

$$\Sigma AB/N = \bar{A}\bar{B} + \sigma_d^2$$

It follows that

$$(\Sigma A^2/N - \bar{A}^2) - (\Sigma AB/N - \bar{A}\bar{B}) = \sigma_\alpha^2$$

and similarly for the second observer, and the probable error of each observer may be calculated. It should be noted that it is implicit in this procedure that $\bar{A}=\bar{D}=\bar{B}$ within the limits of normal error due to the two errors of observation, so that no conclusion is valid if $\bar{A}-\bar{B}$ exceeds twice the value of $\sqrt{(\sigma_\alpha^2 + \sigma_\beta^2)}/\sqrt{N}$

The table below gives the sums for the five measurements of the pelvis, and the work for the conjugate is added as an example

	ΣA	ΣA^2	ΣAB	ΣB^2	ΣB
Conjugate (mm)	3649	445887	444545	443284	3638
Transverse (mm)	3954	522466	522702	523026	3956
Ischial Spines (mm)	3159	334277	334693	335798	3164
Pubo sacral (mm)	3945	521049	417843	515726	3922
Pubic Angle (degrees)	2585	224275	224979	225830	2594

The Conjugate,

$\bar{A}=121\ 63$	$\Sigma A^2/N=14862\ 90$	$\Sigma AB/N=14818\ 17$	$\Sigma B^2/N=14776\ 13$	$\bar{B}=121\ 27$
	$\bar{A}^2=14794\ 67$	$\bar{AB}=14750\ 07$	$\bar{B}^2=14705\ 60$	
	$\sigma_d^2 + \sigma_a^2 =$	$\sigma_d^2 =$	$\sigma_d^2 + \sigma_\beta^2 =$	
	68 23	68 10	70 53	
	68 10		68 10	
	$\sigma_a^2 =$		$\sigma_\beta^2 =$	
	0 13		2 43	
	$\sigma_a =$		$\sigma_\beta =$	
	0 36		1 56	
$0\ 67449\sigma_a =$	0 24		$0\ 67449\sigma_\beta =$	1 04

$\bar{A} - \bar{B}$ is 0 37 and $2\sqrt{(0\ 13 + 2\ 43)}/\sqrt{30}$ is 0 58 so that the method is applicable

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Gangrene Occurring During the Puerperium

BY

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GANGRENE as a complication of the puerperium is noteworthy on account of its rarity, and because of its grave complications

Obscurity surrounds the aetiology of the condition. The more so by virtue of its rarity. It is the purpose of this paper to review all the cases reported in the literature, 110 in all, to add notes on an additional 13 collected from various sources by myself, and 1 case which came under my own care

CASE REPORT

On November 22nd 1940 Mrs X, aged 34 having had one child previously, was admitted to the Cleland Hospital Lanarkshire suffering from phlegmasia alba dolens. She had been delivered 10 days earlier after a normal pregnancy of a healthy full time child the labour being normal.

The previous health and family history were good.

Four days before admission she complained of weakness and cramp like pains in the calf muscles of the left leg with subsequent discoloration of the ankle and swelling of the whole limb. Similar pains developed at the same time in the right leg. On admission her temperature was 101.8°F pulse rate 140, and respiration rate 28. The patient looked extremely ill and very toxic. Her mucous membranes were blanched, and her tongue dry and coated. The left leg was swollen from the groin to the toes and oedema had spread over Poupert's ligaments to fill the left iliac fossa. Both femoral and popliteal pulses were absent and the entire left foot and ankle were dusky to the point of blackness. The foot was cold and anaesthetic to light touch pain and temperature but

muscle joint sense remained. There was also some oedema of the right ankle.

By November 25th a line of demarcation had appeared on the left leg a hand's breadth above the ankle, and the foot showed gangrene of a mixed type. The patient was gravely ill. The right leg however, improved and the oedema subsided. Tenderness was pronounced in the left iliac fossa.

The lochia was normal and the uterus not enlarged. There was no abnormality at any time in the heart so far as could be detected.

Blood culture was negative. The patient died on November 27th.

Summary of Autopsy Report At the post mortem examination 12 hours after death I found considerable hypostatic congestion of the bases of both lungs. The heart and great vessels were normal.

All the abdominal viscera were healthy with the exception of the right kidney which showed a moderate degree of pyelitis. There was marked congestion of the veins of the left broad ligament but they were not thrombosed. The left Fallopian tube was adherent to the left ovarian vein.

The left common iliac, left external iliac and left femoral veins were engorged with organizing thrombus and showed acute thrombophlebitis. There was purulent inflammation of the surrounding tissues.

The left leg was disarticulated at the hip and removed for dissection.

Summary of Dissection The long saphenous vein showed engorgement throughout its length and was filled with organising thrombus which extended into all the larger superficial tributaries. The thrombus was in direct continuity with that of the femoral vein.

The short saphenous vein showed similar

changes, and here the thrombus formation terminated at the junction with the popliteal vein. The femoral vein below the union with the long saphenous vein was quite normal save for a small patch of early thrombophlebitis in its course through Hunter's canal. The popliteal vein was macroscopically normal but the anterior tibial veins showed acute thrombophlebitis as did the posterior tibial veins. The perineal veins were normal to macroscopic examination as were the arteries of the lower limb. There was no history of ergot having been used excepting a dose of the liquid extract 2 drachms, after delivery.

A second case was reported to me by the courtesy of the superintendent of Stobhill Hospital, Glasgow, and Dr Bruce, County Hall, London, made an extensive enquiry over the London County Council Hospitals, and reported 1 case which occurred in St Stephen's Hospital in 1937. This had been investigated in the most minute detail but it is not proposed to recount the result here, rather shall it be considered with the others as a whole.

Lastly, through the kindness of Dr Charlotte Douglas of the Department of Health for Scotland, Edinburgh, facilities were afforded to study the schedules of puerperal deaths for Scotland during the period October 1929 to 1940. Six hundred and seventy-seven schedules were studied for this purpose. The deaths included all those occurring as a result of childbirth, and among them were discovered 11 in which gangrene was present as a terminal event.

Of these 13 cases 11 were fatal. Six occurred in multipara and 7 in primipara, while 1 followed abortion, and 1 a ruptured ectopic pregnancy at the 3rd month. So far as can be ascertained there is no report in the literature of gangrene having followed rupture of an ectopic pregnancy. The condition was preceded by phlebitis of the right foot developing in the 2nd week after operation.

One case followed for Caesarean section, and B. Welchii was here responsible, but the remaining 10 were at term. Sepsis was present in 12 and of the organisms isolated, either from the blood or from the cervix uteri, the most common were streptococci, but B. Welchii was implicated in 4 cases.

DISCUSSION

Analysis of these 124 cases reveals that 111 followed delivery at term, 9 followed abortion, 3 Caesarean section, and 1 a ruptured ectopic pregnancy. Sepsis was present in all the abortions and in 36 of the remaining cases. Information regarding the presence or absence of sepsis is lacking in 50 cases, and in 29 sepsis was not detected.

Ergot or an ergot preparation was definitely a factor of importance in 25 cases, while in 20 of these the drug was administered in the presence of gross sepsis. In one series (Benson's) of 7, ergot preparations in 5 were considered to have played a part.

In at least 5 cases gangrene was a sequel to either thrombophlebitis or phlegmasia alba dolens, in 1 endarteritis was assumed to be the cause (Tol²) and in 2 (King, Miller, Hauser²) it was embolic. Four of the cases were clearly due to the B. Welchii and all of these terminated fatally.

The gangrene most commonly affects the lower limbs but may also affect the upper. In my own series of cases I found the lung, vulva, and perineum affected, and in the cases due to B. Welchii infection, many of the abdominal viscera. That the condition is excessively rare cannot be disputed. Of 148,000 deliveries in the London County Council during a 10 year period, only 1 case of puerperal gangrene could be traced, and of 677 puerperal deaths in Scotland occurring between October, 1929, and

January, 1940, only 11 were complicated by gangrene

SIGNS AND SYMPTOMS

The disease commonly begins between the end of the 1st week of the puerperium and middle of the 4th, and generally affects one or more extremities. The upper limbs are less frequently affected than the lower.

Symptoms and signs of the local condition are those of ischaemia, and occur in the presence of a puerperium complicated by sepsis or debility, rarely in the apparently normal subject. Pyrexia is the rule and the general condition of the patient is bad. She is a poor anaesthetic risk. The gangrene may be of the dry or moist types, and is not infrequently mixed.

The lochia is often slightly offensive, and the uterus usually shows a degree of subinvolution, while slight lower abdominal pain may add to the patient's misery.

The patient is usually a multipara, and frequently the antenatal period and delivery have been normal.

TREATMENT

Prodromal signs suggestive of imminent vascular obstruction developing during the puerperium indicate that the limb should be kept warm and completely at rest.

If there is any suspicion that ergot or its preparations have been used in appreciable doses the drug must be stopped and acetylcholine substituted for it.

Attention must be directed to the uterus itself, and any local septic condition dealt with vigorously. The same applies to any obvious point of focal sepsis generally.

Should phlegmasia or thrombophlebitis be present, amputation should not at once be performed, but expectant measures adopted until the local condition has improved and a clear line of demarcation formed. When the general con-

dition warrants amputation this may be carried out at the site of election, bearing in mind that the patient is a poor risk and that speed is essential.

Prophylaxis Ergot should not be used in the presence of sepsis.

PROGNOSIS

Of a series of 83 cases in the literature 44 ended fatally, and of those which recovered, only 4 avoided amputation. The condition lasts a varying number of days, but if death supervenes it does so frequently after 7 to 10 days, while if amputation is carried out at the optimum moment, when the general condition is improving, the outlook is improved.

The prognosis is also improved by conservative treatment in the first instance.

AETIOLOGY

Several theories have been advanced. Rosenow⁴ in 1927 described a haemolytic streptococcus associated with diplo streptococcus in 1 case, which, when injected into animals caused a loosely attached thrombus to form in the large vessels. King, Miller, and Hauser likewise isolated a diplo streptococcus from thrombus present in the veins of their patient. These are the only reported attempts to investigate the bacteriology of the thrombus, and more work along this line might be productive of useful information.

Stein⁵ believed that there may be a lesion of the vascular endothelium due to the action of toxins from bacteria, in addition to the altered state of the blood during the puerperium predisposing to thrombus formation. This also is in accord with the views of Rosenow. Here it is worthy of note that sepsis need not be confined to the uterus or adnexia. Focal sepsis, for instance, in tonsils and nasal sinuses, could provide the necessary reservoir of toxins.

The part played by ergot and its preparation is of interest. In the case reported to me by Dr. Bruce, ergot was clearly the cause. Yater and Cahill,⁷ Saenger,⁸ McNalley,⁹ and Roche¹⁰ also attribute the gangrene to the use of ergot in cases seen by themselves. It is however certain that although ergot can and does, on occasion, cause gangrene it does not account for the vast majority of the cases under discussion.

A matter of interest is that varicose veins have seldom been present, and that the Wassermann reaction is usually negative, thus ruling out the effect of the spirochæta on the vessel walls as a predisposing factor.

There are several ætiological factors and these may be considered as follows:

1. *Predisposing causes.* Of these, sepsis is dominant and was present in gross form in 45 of the total series of 124. It was considered to be absent in 29, and in the remaining 50 information was lacking.

Secondly may be considered all debilitating conditions, and of these anaemia is the most important. It is accepted that in anaemia blood coagulation is hastened.

2. *Precipitating causes.* The site may be determined by trauma, by local thrombosis, thrombophlebitis, or phlegmasia alba dolens, but in a considerable number of cases the precipitating factor has not been obvious.

The use of ergot in the presence of sepsis may act as specific in a number of instances.

It is possible that a specific micro-organism with an elective affinity for walls of the blood vessel may be the cause in a number of cases.

Lastly, a small group of patients develop gangrene during the puerperium as a result of embolism.

On the basis of the information to hand it is not possible further to suggest the cause

of this affection, and additional research with a larger series of cases will be necessary before more definite conclusions can be reached.

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Observations on Shute's Test for Anti-Proteolytic Properties
of Human Blood Serum in cases of Abortion,
Premature Labour, Accidental Haemorrhage and
Normal Pregnancy

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INTRODUCTION

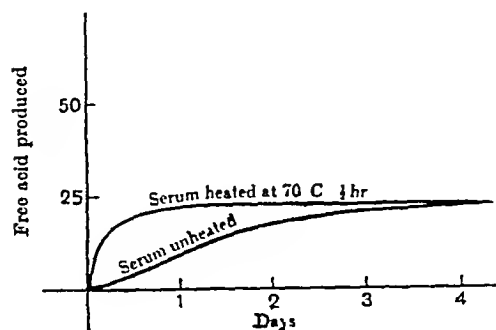
SINCE 1935 Shute¹ has published an interesting series of papers describing an anti-proteolytic power exhibited by the blood serum of women in whom abortion, premature labour, accidental haemorrhage or some of the toxæmias of pregnancy occurred. This anti-proteolytic power is said to be due to excess oestrin in the blood and is often associated with vitamin E deficiency. Shute claimed that these accidents of pregnancy could frequently be prevented by suitable vitamin E therapy. If these claims could be substantiated a tremendous advance in the treatment of many types of abnormal pregnancy would be achieved. Shute's test is based on work published by Wigglesworth and by Fine which may be briefly summarized as follows.

In 1928 Wigglesworth² described observations by Cole that when proteins were acted on by proteolytic enzymes the amount of standard alkali required to titrate the mixture to an arbitrary pH (say pH 8.4) is found to increase as the digestion proceeds. The acidity so measured is termed "free acidity." If the mixture were

then treated with neutral formaldehyde the reaction became acid and further additions of standard alkali were necessary to bring the mixture back to pH 8.4. This latter acidity is termed "formaldehyde acidity." In the case of the proteolytic enzyme trypsin, the "free acidity" is produced more rapidly in the early stages of digestion but soon reaches a constant level whereas the "formaldehyde acidity" continues to increase.

In 1931 Fine³ in determining the influence of serum on enzymes, with special reference to its action on trypsin, showed that serum heated at 70°C. for half an hour behaved differently from unheated serum when each was incubated with trypsin. From his experiments he concluded that "serum possesses a property destroyed by heat, of temporarily retarding the formation of free and formol acid by trypsin, and of subsequently accelerating the formation of formol acid only." Trypsin is stated to consist of two enzymes (a) protease giving the rise in free acid and (b) peptidase producing the increase in formol acidity. The serum acts against the protease portion of the trypsin. Fine suggests that the free acid is formed as the result of hydrolysis of non-amide linkages, e.g. ester linkages in the

protein molecules. A typical free acid curve is shown in Graph 1.



GRAPH 1

Free acid produced in digestion of 10 per cent serum by 10 per cent trypsin. This shows how free acid produced by inhibited trypsin ultimately equals amount formed by uninhibited trypsin.

This graph is taken from: On the Influence of Serum on Enzymes with Special Reference to its Action on Trypsin. By Joseph Fine from the *Biochemical Journal* Vol. XV Part 1, 1931, page 625.

Shute incubated 0.5 c.c. serum from freshly drawn blood in 3.5 c.c. Kolthoff buffer at pH 8 with 1.0 c.c. trypsin solution (0.002 per cent) at 32° to 42°C. At 10 minute intervals 0.5 c.c. of the mixture was removed and added to 5 c.c. distilled water containing 5 drops of phenolphthalein. The samples were titrated against freshly prepared N/100 sodium hydroxide, the end point being determined by comparison with 1.0 c.c. Kolthoff buffer at pH 9, containing 10 drops of phenolphthalein. With serum from normal patients typical curves were obtained when the volumes of N/100 sodium hydroxide were plotted against the time (Graph 2).

Very different curves were obtained in similar experiments in which the sera tested were obtained from women in whom abortion, miscarriage, premature labour and accidental haemorrhage had occurred. In such cases the normal action of trypsin was inhibited for longer than 40 minutes, after which time the normal digestion with liberation of free acid took place. Shute carried

out parallel experiments on each serum, one sample being heated for 30 minutes at 55°C, the other being left unheated. Three types of results occurred with these experiments on the same serum.

(a) Inhibition of digestion of both heated and unheated samples.

(b) Inhibition of digestion of the unheated sample.

(c) Inhibition of digestion of the heated sample.

(See Graph 3.)

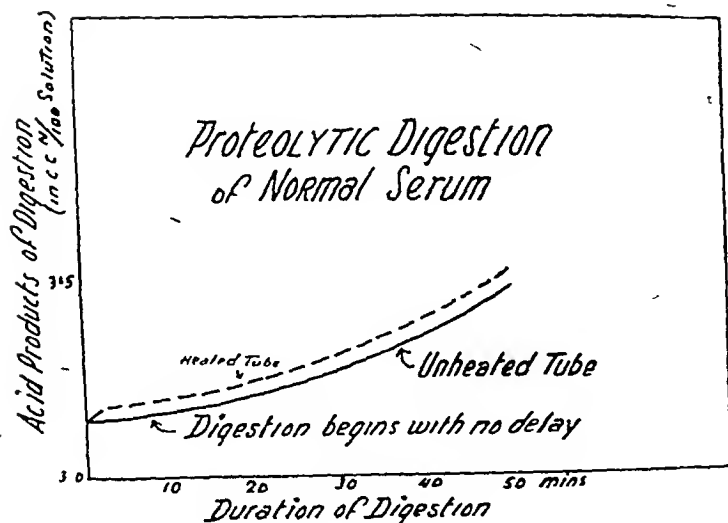
Shute interpreted each of these three types of results as representing inhibition of proteolysis. Sera giving such results lost their anti-proteolytic activity in from 24 hours to 12 days after removal of the blood from the body. In some patients anti-proteolytic power was detected 6 weeks before abortion or other of the specified conditions occurred. If the uterus were curetted the anti-proteolytic power of the serum disappeared rapidly, usually within 2 days, while in spontaneously aborting patients the blood became normally digestible a few days after abortion.

A comparison of the work of Shute with that of Fine shows several outstanding differences.

(a) With approximately similar concentrations of serum, Fine uses a very much greater concentration of trypsin, yet the free acid production is of the same order as that found by Shute.

(b) While free acid appears to be liberated within 40 minutes in Shute's experiments, graphs in Fine's paper show a gradual rise to a maximum over several hours.

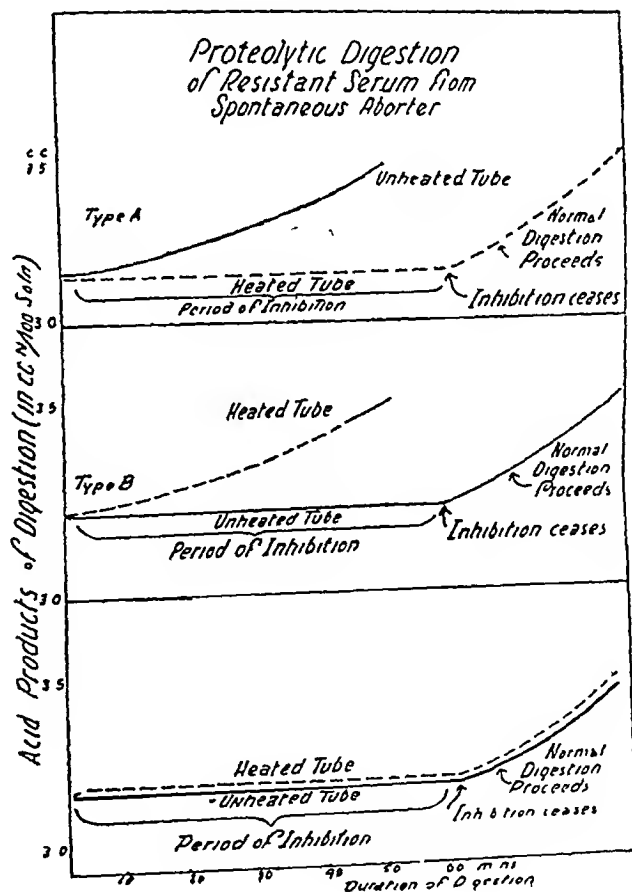
(c) Fine observed that heating removed inhibitory substances from serum so that the free acid was always liberated more rapidly in the heated specimen. In Shute's experiments the results obtained bore no



GRAPH 2

Illustrating the digestion of a normal serum with and without preliminary heating by a solution of trypsin

RESISTANCE TO PROTEOLYSIS



GRAPH 3

Illustrating various types of digestion of resistant or inhibitive sera with and without preliminary heating by a solution of trypsin

These graphs are taken from Resistance to Proteolysis found in the Blood Serum of Aborting Women By Evan Shute *The Journal of Obstetrics and Gynaecology of the British Empire* Vol 42 1935 page 1076

constant relation to whether the serum was previously heated or not

In spite of these contradictions the obvious advantage of being able to detect the possibility of disturbances of pregnancy prior to their occurrence was so great that it was decided to investigate sera from various types of patients by this method. Tests were performed on sera from 85 patients including normally pregnant women, and those in whom abortion, premature labour and accidental haemorrhage occurred. Several different samples of serum from the same patient were examined in some instances to determine if variations occurred in serum from the same individual.

1 INVESTIGATION OF METHOD

In testing Shute's method it was found impossible to obtain consistent results for titrations of free acid against N/100 sodium hydroxide using phenolphthalein as indicator by matching the end point with 10 c.c. of Kolthoff buffer pH 9 containing 10 drops of phenolphthalein. Similar difficulty has been reported by Cuthbertson and Drummond,⁴ and they used an achromatic indicator with much greater success. This indicator has been found very satisfactory throughout this

series of tests. It consists of a mixture of methyl red, methylene blue and phenolphthalein and when added to the water and digest the mixture is clear green. On addition of alkali the indicator goes through a grey shade and finally changes to a violet colour which is matched in a pH comparator with the colour developed in 10 c.c. of Kolthoff buffer at pH 9 containing an equivalent amount of indicator. The maximal difference between five consecutive titrations on buffer serum mixture was 0.1 c.c. N/100 sodium hydroxide.

2 EXPERIMENTAL RESULTS

(1) Tests on sera from different types of patients

The action of trypsin was tested on sera from 37 normally pregnant women, from 33 women with toxæmias of pregnancy and from 15 women who had threatened abortion, abortion, premature labour or accidental haemorrhage. The results are summarized in Table I.

In 39 experiments there was an increase in free acid during the incubation period, and in 37 others in which the initial acid concentration was greatest the curves showed a downward trend. In 9 cases there were only slight variations in free acid concentration during the experiment.

TABLE I

Results of tests for antiproteolytic activity				
Type of patient	No	Increase in free acid within 40 minutes	Decrease in free acid within 40 minutes	No change in acidity
Normally pregnant women	37	19	18	—
Toxaemic pregnant women	33	12	13	8
Women with abortion, premature labour, or accidental haemorrhage	15	8	6	1
Total	85	39	37	9

Only 11 of the 85 curves obtained bore any resemblance to those described by Shute. The rise in acid in the other 28 experiments in which an increase occurred within 40 minutes was usually quite rapid and was followed, in nearly every instance, by a sharp fall. Frequently there was a second rise and sometimes a subsequent fall. The curves were, in general, more like those described by Fine (see Graph I). This resemblance is only a superficial one since his experiments showed the effect of trypsin over a period of several days and the maximal action appears to have taken place during the first 6 hours, while the acidity, in this series of experiments, reaches a maximum within 40 minutes. The curves, therefore, are hardly comparable.

In addition to adhering closely to Shute's method, samples were tested immediately after the various constituents were mixed and also after 5 minutes incubation at 37°C. This procedure was adopted since Wunderly⁵ using a nephelometric method, claimed that the main action of trypsin on serum proteins resulting in liberation of free acid took place within 15 minutes. When readings at zero and 5 minutes were included in the series, tests on 35 of the normally pregnant women were classified as follows:

Rise in free acid	11
Fall „ „ „	13
No change „ „	11

Many of the 19 tests in the normally pregnant group, previously showing a rise in acidity were now characterized by a fall and then a rise, and in some instances by a further rise and fall within 40 minutes. Similar curves were obtained for the action of trypsin on sera from toxæmic patients and from women having abortion, premature labour and accidental hæmorrhage. Many of the tests were prolonged to 100 minutes and the curves were similar to

those already described. Examination of the results obtained with this test indicated such irregularity that it seemed very doubtful whether the curves obtained were really due to liberation of free acid by the trypsin extracts. For this reason it was decided to test the effects of variation of a single constituent or groups of constituents. Firstly, tests with different samples and concentrations of trypsin were investigated, and secondly, the effect of incubation on various constituents of the final digestion mixture were examined.

(2) *Effect of Variation in Constituents of Digestion Mixture in Shute's Test*

(a) *Tests with different samples and different concentrations of trypsin*. Three different samples of trypsin, each of which had been shown to digest fibrin in alkaline medium, were used in the preparation of solutions for these experiments. Not only was the trypsin used in a concentration of 0.002 per cent as specified by Shute, but in some instances concentrations of 0.01 per cent and 0.05 per cent were substituted. The results did not seem to vary with the concentration or the sample of trypsin used. These observations confirm those of Cuthbertson and Drummond.

(b) *Effect of incubation on buffer solution and mixture of buffer with the various substances used in Shute's test*. In order to test the effect of incubation on buffer solutions and on mixtures of buffer solution with the various substances used in Shute's test, duplicate tubes were set up containing

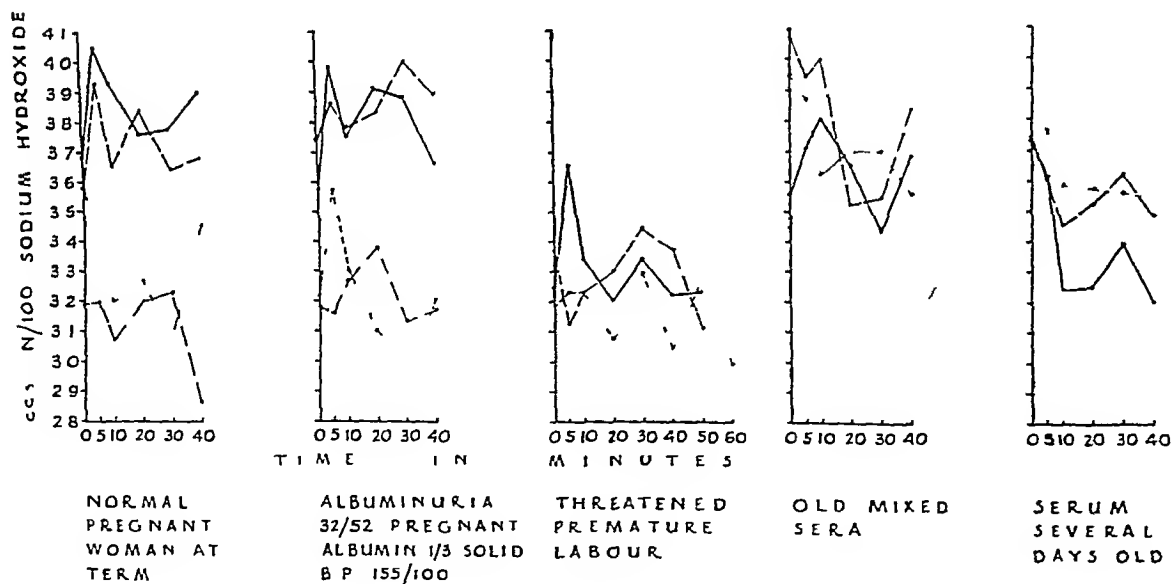
- (1) Kolthoff buffer solution at pH 8 and water
- (2) Buffer solution at pH 8 and trypsin
- (3) Buffer solution at pH 8 and serum
- (4) Buffer solution at pH 8, serum and trypsin.

- (5) Buffer solution at pH 8, serum and trypsin heated in a boiling water bath for at least 30 minutes

Constant volumes were attained by the addition of distilled water to the tubes containing fewer ingredients. Duplicate experiments on each mixture agreed very closely. Characteristic examples of curves obtained in experiments using the various mixtures specified are illustrated in Graph 4.

solution were titrated against N/100 sodium hydroxide. Somewhat greater variations occurred when buffer trypsin mixture was similarly tested. Marked variations occurred when serum from normally pregnant women and buffer were tested, but addition of trypsin to the mixture before incubation caused no increased effect. As a final control the action of trypsin and inactivated trypsin on the same sample of normal serum in buffer solution

- Buffer
- - - Buffer + Trypsin
- Buffer + Serum
- Buffer + Serum + Trypsin
- - - Buffer + Serum + Heated Trypsin



GRAPH 4

These graphs show that even when the buffer solution alone was incubated at 38°C, and samples were removed and titrated under the same conditions as were used in Shute's test, greater fluctuations occurred than those obtained when successive, measured samples of unincubated

gave almost identical results. The types of curves in these experiments were similar to those obtained in the series on sera from different types of patients and again there was no possibility of correlating a special type of curve with any combination of constituents in the mixture being tested.

CONCLUSIONS

Incubation at 38°C of the serum of pregnant women with trypsin in buffer solution at pH 8 resulted in variations of free acid during a period of 40 minutes but there was no consistency in the type of curve obtained by estimation of free acid at regular intervals. Prolongation of the test to 100 minutes did not affect the types of curves obtained. The results do not support claims recently made by Shute that free acid is liberated under the above conditions within a period of 40 minutes. In some cases there is an increase, in others a decrease and in some instances there are only slight fluctuations in acidity of the incubated mixture.

The experiments show that slight variations occur without serum and it can be definitely stated that the variations are not a tryptic effect since serum and buffer, serum, trypsin and buffer, and serum, inactivated trypsin and buffer each give almost identical curves.

In our experience serum from neither normal nor abnormal patients showed

evidence of digestion by trypsin under the conditions specified.

The observations recorded in this paper together with the results of Cuthbertson and Drummond indicate that Shute's test for inhibition of proteolysis is not a satisfactory means of distinguishing women in whom abortion, miscarriage, premature labour or accidental haemorrhage is likely to occur from those whose pregnancy is likely to pursue a normal course.

ACKNOWLEDGEMENT

This work was carried out under grant from the National Health and Medical Research Council of Australia.

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Chorionepithelioma (Some Observations)

BY

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THE pathology and progress of this malignant tumour are so well known, and have so often been described, that at first sight it would not appear necessary to add to its already voluminous literature. However, personal observations may often prove to be of value and interest so it is for these reasons that the authors of this short paper venture to record their observations.

It is an established fact that the tumour starts as the result of over activity of the trophoblastic element of the growing human ovum, and no other theory for its genesis is tenable. Its continuance of growth is dependant upon the life of its embryonal elements, and as long as these remain alive so long does the tumour increase in size. The Aschheim-Zondek and Friedman tests are the most valuable aids to the clinician in this disease for it is well known that the tests become negative some 3 weeks or so after the death of the ovum, owing to the withdrawal of the anterior pituitary like hormones from the urine of the patient.

What is it that causes the trophoblast

suddenly to become so excessively active? No one at present knows. Will the secret ever come to light? At present it is as elusive as the etiology of other forms of cancer. It is suggested that it may be due to persistence of corpus luteum hormone, this is reasonable when one realizes that there is excessive luteinization of the follicles in association with moles and chorionepithelioma¹. Though chorionepithelioma may follow on any pregnancy, yet it is most common following on cases of hydatidiform mole and abortion². Hydatidiform mole is a cystic degeneration of the chorionic villi of the ovum, and so is definitely a pathological condition of the products of conception and one, therefore, ready and potent to grow into a neoplasm. But why does it not always do so? Abortion may be caused by reasons other than pure pathological conditions of the ovum. Does chorionepithelioma arise following abortions due to non-pathological disease of the ovum? The answer is, frequently yes but it occurs less frequently following abortion than in conjunction with

a mole, and the neoplasm may occur following a full-time pregnancy. The tumour is situated usually in the uterus, but may occur primarily in the vagina, or Fallopian tube.³

It is stated that the growth may arise shortly after the termination of the pregnancy, or may not appear for several months or even years afterwards.⁴ The authors do not agree with the latter part of this statement and are confident that in patients in whom this seems to have been the case that another, unrecognized pregnancy of short duration has occurred. It is noteworthy that this is in agreement with some of the later textbooks.⁵ It is also stated that the tumour usually is of rapid growth but may grow very slowly.

The tumour grows by means of the invading property of the trophoblast, the latter element burrowing deeply into the musculature of the uterus. The endometrium is not invaded by the growth. The trophoblast has already invaded the endometrium in order to form the decidua, but when the chorionepithelioma starts, the endometrium is not further invaded. The essential pathology is an invasion of the deeper structures.

The clinical symptoms so quickly follow a history of an interrupted pregnancy that it is a reasonable supposition the trophoblast grows rapidly, sometimes more rapidly than at others, but we have not been able to find evidence of the "slow growth" described by some writers.⁶ Having observed personally several cases during the last 3 years, we cannot bring ourselves to accept the theory that a long interval may elapse between the pregnancy and the onset of the growth. We consider that though the patient and/or her relatives may honestly believe that there has not been a pregnancy for some time, careful questioning will elicit the fact that a short while before the onset of symptoms of the

disease, an excessively heavy period took place, or there was a sudden haemorrhage *per vaginam*. This, of course, being a succeeding pregnancy and the direct precursor of the tumour.

We consider that the trophoblast will not invade the uterine tissue to a certain distance and then become dormant only to wake up some time later. The Aschheim-Zondek test would be conclusive evidence, but in the absence of symptoms it is not demanded, and one cannot subject patients to this test, at various times after every pregnancy for many reasons, though no doubt scientifically it would have many adherents. It is interesting to note that as metastases occur, so does the Aschheim-Zondek test become stronger.

For the most part the history of our cases is fairly typical, and pathologically unmistakable. Only one of our cases displayed an extension of the disease, which in this patient invaded the vaginal vault and bladder.

Many authorities, notably Wilfred Shaw and Beckwith Whitehouse comment on the extreme rarity of the condition, which is probably the case in some parts of the world, but in the Eden Hospital it is found to occur as frequently as 0.262 per cent of all gynaecological cases admitted, the number of cases reviewed in this paper being 14 out of a total of 5,712 patients admitted over a period of 3 years. This percentage is higher than most authors state. In 8 of these cases a hydatidiform mole preceded the chorionepithelioma. It is not necessary to give in detail the history of each individual case, but one abridged typical average history is appended, and the abridged histories of 4 special cases. All the cases displayed the usual well-known symptoms of the disease, i.e., the haemorrhage, necrotic sero-sanguinous discharge, or when metastases occurred, the typical emaciation, and cachexia.

CASE 1 An average typical history

Mrs P D (Indian) age 23, 3 para History of having expelled a mole 3 months ago Within one month bleeding started Curettage not advised Total hysterectomy performed Result—a typical chorionepithelioma

CASE 2 Mrs G (Indian), age 23 3-para History of expulsion of a mole 10 years previously Since then had 2 normal pregnancies, last one 2 years before admission Aschheim-Zondek test positive Hard lump in lower abdomen

Hysterectomy, result chorionepithelioma It is considered there was a recent pregnancy to account for this condition

CASE 3 Mrs P (European) age 40 Married 16 years no pregnancy Admitted with a history of having missed a period then after 12 days had severe bleeding *per vaginam* The uterus was enlarged to the size of a 7 weeks pregnancy Patient was curetted Scrapings showed malignant chorion hysterectomy revealed a chorionepithelioma

A very interesting case of the disease occurring in an elderly primipara

CASE 4 Mrs M (European) age 30 4-para Admitted for hyperemesis gravidarum Treatment of little avail so uterus evacuated The pregnancy was a mole After 4 weeks bleeding began *per vaginam* Aschheim-Zondek test not done as no facility at the moment Hysterectomy performed and the result was a chorionepithelioma

An interesting case demonstrating the the extreme rapidity of the growth

CASE 5 Mrs M B (Indian) age 24 9 para Uterus the size of 24 weeks pregnancy soft no foetal parts While being examined there was a sudden rush of blood Uterus immediately emptied of a mole Discharged from hospital on August 29th, 1941 Re-admitted on September 1st 1941, with history of bleeding from the day before Hysterectomy carried out next day Chorionepithelioma was found

There are some interesting points about some of these cases Case 3 was a great personal friend of one of us (H E M), who had known her for years It was, therefore,

with astonishment that he recognized her state of pregnancy after so many years of sterility, and it was with consternation that he realized a hysterectomy was necessary It was with dismay that the patient and her husband learnt of the decision, but they understood at once the gravity of the case and agreed to immediate operation, with the result that the lady is now quite well 3 years after the operation

Case 4 This is a sad case, as the patient developed a secondary or implantation growth in the vault of the vagina before she had got as far in her convalescence as getting out of bed The growth involved the bladder so that a vesico vaginal fistula appeared The patient's husband was told of the gravity of the prognosis so he decided to remove her to Bombay where her parents lived

Case 5 The interest of this case lies in the fact that the radical operation was performed very early Macroscopically it was difficult to make out a tumour at all There was just some thickening The microscope, however, revealed in full the malignant state

TREATMENT

The essential treatment is surgical Hysterectomy should be carried out as soon as the condition is diagnosed, and this is followed in 3 weeks by a course of deep X-ray therapy The ovaries may or may not be conserved Some surgeons advocate leaving them in position as ovarian metastases are rare, but if in order to do one's best for one's patient, deep X-ray therapy is administered after the operation, the ovaries will be rendered inert, so it does not seem a sound surgical procedure not to remove the ovaries at the operation

There are certain aspects in the treatment of chorionepithelioma It is spontaneously cured more often than any other known

malignant tumour. Specially after hysterectomy, secondary growths have sometimes disappeared without treatment. But once the resistance to its spread is broken down it runs a more rapid fatal course than any other new growth. After diagnosis is made either clinically, microscopically or by Aschheim-Zondek test in higher dilution, immediate hysterectomy with removal of appendages is necessary. In some clinics, intrauterine radium has been tried. The opinion is unanimous regarding removal of the cystic ovary. In young patients, the other healthy ovary can be left alone, but in patients above 40 both ovaries should be sacrificed. During operation, ovarian and uterine vessels should be ligated or clamped early to prevent dissemination. Deep X-ray therapy of the abdomen and pelvis is to be followed as a routine. Aschheim-Zondek test during treatment is a guide to the cure.

Our observations may be summarized as follows

1 The most complete uniformity of history and symptoms. That is, haemorrhage *per vaginam* commencing soon after the termination of treatment for the removal of products of conception, whether mole, abortion or later pregnancy, or following on an excessively heavy period. In only one case was there a history of a long period of time since the last pregnancy or heavy period.

2 The rapid rate of growth of the neoplasm. This was noted by observing the size of the tumour in relation to the duration of symptoms.

3 The high degree of malignancy. This was noted by the invasion of the tissues as seen microscopically, having due regard to the duration of the symptoms.

4 The excellent response to treatment when uncomplicated by metastases.

5 The deleterious effect that metastases caused.

6 The extreme usefulness of the Aschheim-Zondek test. Actually the Aschheim-Zondek test was not the one carried out by us owing to the difficulty of getting mice. We used the Friedman test, but this also was not always possible. The Hospitals and Institutions in India have not got the large animal departments which exist in other places, so that animals are not kept and bred on the spot, and so ready for use at any time. On each occasion the rabbits had to be acquired specially, which meant extremely careful preliminary watching of the animals.

Our thanks are due to Dr B P Tribedi, M B, D B (Lond), Professor of Pathology, The Medical College, Calcutta.

To Dr S Hazra, L R C P, M R C S (Lond), F R C S (Edin), Registrar, The Eden Hospital, Calcutta, for the notes of the cases.

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Multiple Primary Cancers of the Uterus

BY

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CULLEN¹ devotes a chapter of his work on "Cancer of the Uterus" to the 'Coincident Appearance of Carcinoma in the Cervix and in the Body of the Uterus,' but after reviewing the 6 cases which were then on record, decided that not one of them provided conclusive evidence of multiple primary malignancy. He points out that before such an assumption is justified, the possibility of one growth being a direct extension or a metastasis of the other must be excluded, and in the uterus this is often difficult.

A uterine carcinoma may penetrate the myometrium to appear on the mucosa at some distant point, and Jellett² has recorded such a case in which fundal and cervical growths, separated by normal endometrium, were shown to be connected in the uterine musculature. A corporeal cancer may be responsible for a cervical metastasis either by retrograde lymphatic flow, or by the implantation of carcinomatous fragments in the mucosa of the cervical canal. It is also acknowledged that extension of carcinoma of the cervix by metastasis, both into the substance and also into the mucosa of the corpus is not rare.

It is evident, therefore, that before two cancers occurring in the same uterus may be regarded as separate malignant processes, they must possess distinct histological characters. They must, moreover, arise in different situations and be clearly

independent. Carcinomata composed of an admixture of glandular and squamous elements do not enter this category. Irregular areas of epitheliomatous tissue are commonly seen in corporeal adenocarcinomata, particularly in those of the lower degrees of malignancy, and adenocarcinomata have also been described in the cervical canal and portio. The adenocarcinoma usually constitutes the bulk of the tumour, but occasionally the squamous portion of the growth is predominant. Adeno-acanthomata are now regarded as single tumours, in which certain of the cancer cells have displayed an extreme power of polymorphic growth.

The following case is presented as one of double primary uterine carcinoma, in which the above criteria in regard to locality and histological type, are fulfilled.

Mrs G. H. 47 years of age, was admitted to the Cardiff Royal Infirmary in September 1941. She had one child, 11 years old and complained of continuous vaginal bleeding for 9 months and more recently of lassitude, weakness and considerable loss of weight. On pelvic examination it was noted that a bleeding, soft, friable, polypoid mass filled the cervical canal and was presenting at the widely dilated external os. The vaginal surface of the cervix was healthy. The body of the uterus was slightly enlarged and firm in consistency. As the case was regarded as one of corporeal cancer, the uterus was removed together with the appendages and a segment of the vagina. Convalescence was uneventful.

PATHOLOGICAL DESCRIPTION

The uterus was uniformly enlarged, and with the cervix measured 9.5 by 8 by 5 cm. The appendages were normal. The specimen was bisected antero-posteriorly, and showed the appearance presented in Fig. 1.

The entire corporeal endometrium is involved in a diffuse type of adenocarcinoma, and presents a thickened, irregularly polypoid appearance. There is no macroscopic penetration of the myometrium, but histological examination reveals scattered deposits of adenocarcinoma deep in the uterine wall. The growth is characterized microscopically by enlarged glands lined by several layers of cuboidal and cylindrical cells with dark hyperchromatic nuclei (Fig. 2).

The cervical canal is occupied by an exophytic squamous-cell carcinoma measuring 4.5 by 4 by 2.5 cm., growing from its anterior wall. The tumour has a narrow base, and here invasion of the cervical musculature is evident to the naked eye as a translucent greyish white area (Figs. 1 and 2b). Patches of necrosis are visible in the lower pole of the tumour. Microscopically, the growth is composed of round and polyhedral cells, without pearl formation or keratosis (Fig. 3). Prickle cells were not seen.

The boundaries of the squamous and glandular cancers are shown diagrammatically in Fig. 4. The demarcation of the tumours was clear cut, and any suggestion of transition from one to the other could not be detected.

MULTIPLE PRIMARY MALIGNANCY

The occurrence of multiple primary malignant tumours in the same individual has been a subject of considerable interest

for many years. Until the beginning of the present century, it was regarded as an extremely rare phenomenon, but the more complete investigation of neoplastic diseases of recent times has resulted in numerous reports of larger or smaller series of cases of this condition.^{3, 4, 5} Warren and Gates¹ found 40 instances of multiple primary malignancy in the course of 1,078 postmortem examinations on patients dying of malignant disease, and after an exhaustive search of the literature collected and analysed a total of 1,259 cases. These authors came to the conclusion that multiple primary malignant tumours occurred more frequently than could be explained on the basis of mere chance, and this view has since been supported by Bugher⁶ and Burke.⁷ These statistical studies have also shown that the incidence of multiple primary malignant tumours in paired organs (breasts, ovaries, testes) and in functionally related organs (breast, ovary, uterus) is much greater than the normal expectancy.

Multiple malignant tumours of the same organ is much more rare than the incidence in different organs of the same individual,^{1, 5} with the exception of the skin, where Ward found 5.3 per cent of rodent ulcers to be multiple.⁸ Other organs affected by multiple primary malignant tumours, in order of frequency, are the large intestine, pharynx and stomach.⁴

There are relatively few reports of multiple primary malignant tumours occurring in the uterus, where it seems that the most common combination of malignant tumours is that of carcinoma and sarcoma. Hertel⁹ found carcinoma of the cervix in 8 of 29 cases of uterine sarcoma.

The simultaneous growth of two carcinomata with distinct morphological characters in the same uterus is very rare, and according to Frank,¹⁰ there was no case on record in 1931. In 1935, Gold-



FIG. 1

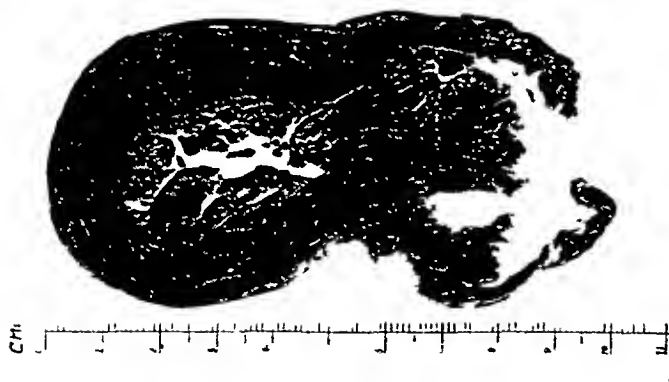


FIG. 2

R. C. M.

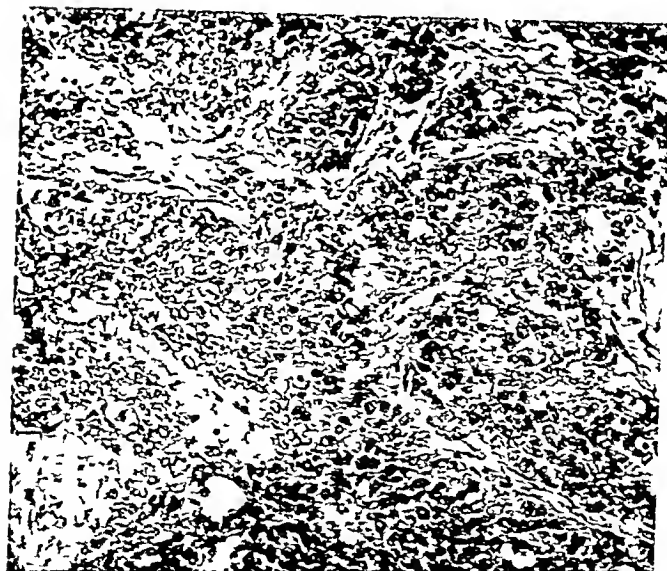


FIG. 2

R C M

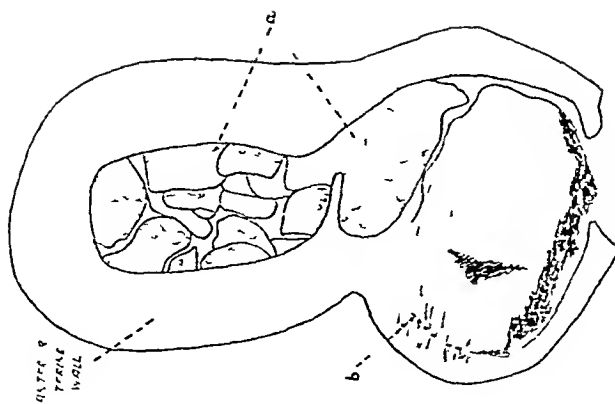


FIG. 1

a Adenocarcinoma
b Squamous cell carcinoma

stine¹¹ reported a case of squamous carcinoma of the portio and adenocarcinoma of the fundus. In 1936, Counseller and Butsche¹² describes 2 cases—one in which a mixed epithelioma and adenocarcinoma was found at the internal os, and an adenocarcinoma in the left cornu, and their second case presented a combination of adenocarcinoma, grade 3 of the cervix and adenocarcinoma grade 2 of the fundus. In 1939, Smith and Masson¹³ recorded a unique case of epithelioma of the cervix and an adenocarcinoma arising in a uterine adenomyoma.

The main interest of studies in multiple malignancy lies in the light they may shed on individual resistance or susceptibility to cancer, and to the rôle played by heredity in this disease. They indicate that an individual affected by one malignant tumour provides fertile soil for the development of other dissimilar tumours, and these occur too frequently to be regarded merely in the light of coincidence. This may imply, as Bugher suggests, that the risk of acquiring cancer is not spread uniformly over the entire population, and that only a certain section of it either has a susceptibility to the disease, or is exposed to some influences favouring its development.

When two primary tumours affect the same organ, Ewing¹⁴ considers that in some cases, the second tumour may result from local conditions brought about by the presence of the first. In almost all reports, multiple primary malignant tumours of the uterus were synchronous, and were recognized after hysterectomy, but recently Jacob, Major and Baker¹⁵ described a case in which a mixed tumour composed of adenocarcinomatous, epitheliomatous and sarcomatous elements developed in the lower segment of the uterus, 16 years after an epithelioma of the cervix had been successfully irradiated. The risk of an indi-

vidual affected by one cancer, developing another independent malignancy in later years is substantially reduced by the short expectancy of life caused by the first tumour. The risk of such an occurrence in the same organ, such as the uterus, has in the past been largely eliminated by the surgical extirpation practised for the initial malignancy, but with the wide adoption of radiotherapy for uterine cancer, it is probable that metasynchronous primary malignant tumours of the uterus will be more frequently observed.

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Photograph taken post mortem showing destruction of limbs, facial and perineal areas, exposure of rectum and invasion of vulva into anus

J B D

Pregnancy and Labour Complicated by Ascending Myelitis and a Bed sore of Unusual Size

BY

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THIS case is reported because it must be of unusual occurrence and, therefore, possibly of general interest

The patient was a multipara of 43 years of age, having had 4 children previously. Her pregnancies were normal except for the fourth during which she developed toxæmia of such severity that induction of labour at the 38th week was necessary. She was first seen on April 26th, 1940, after admission to hospital with unusual abdominal distension, abdominal pain, incontinence of urine and some oedema of feet and ankles. She was 18 weeks pregnant.

On examination the abdomen was found to be larger than usual for the duration of the pregnancy, being also hard, tense and painful. This condition was due to distension of the bladder with incontinent overflow. Slow emptying of the bladder relieved the abdominal signs and symptoms but the distension and incontinence recurred. Loss of power and sensation was noticed in the feet and the case appearing to be one of central nervous lesion it was transferred to the physicians.

Under the care of Dr Smirk, the Professor of medicine, the patient's condition was declared to be one of rapidly ascending myelitis of obscure cause. The distribution of the elements of the spinal cord stopped at the level of the 4th dorsal vertebra, but below this there was complete loss of sensation and motor power. Nearly 4 months later the patient was returned to the obstetrical department for delivery. In the interval she had deteriorated and unfortunately had now a bed sore of quite

unusual size and severity. Her temperature was normal, her pulse-rate 120, her respirations 30. The urine was free from albumin.

The pregnancy had now reached 35 weeks, the presentation was cephalic and foetal heart sounds audible. On inspection the bed sore extended from the lumbar region to the vulva. All tissues superficial to the sacrum, rectum and perineum had been destroyed, the rectum was exposed down to its muscular coat and the posterior commissure of the vulva reduced to an intact band of skin not more than 20 millimetres in width. Laterally the sore involved the buttocks and the gluteal muscles were exposed and pendulous in the edges of the sore.

More by good fortune than by judgment it was seen, at the same time, that the foetal head was so low in the vagina that the scalp was already showing at the vulva, completely painless labour having been in progress for some indefinite time. The birth of the child was completed in a few minutes without pain, the mother being unaware of the birth. The child was premature and small so that, fortunately, the narrow circumferential ring of vulval skin was undamaged. Uterine contractions of the 3rd stage were vigorous and the placenta was quickly expelled without any loss of blood. The child, a male, weighing 4 pounds 4 ounces, was alive and has since thrived. Immediately after the delivery the mother appeared to be in fair condition but an hour later she collapsed and died.

BOOK REVIEW

Progesterone (Pregnandiol) and Oestrogen in Pregnancy "

A M HAIN who previously (*Journ Endocrinol* 1940 11, 104) investigated the output of pregnandiol and of the two combined oestrogens in women approaching parturition and in one person throughout normal pregnancy has now* examined the hormone output associated with abortion. The first part of her paper concerns five women in whom oestrogen and pregnandiol outputs were measured at very frequent intervals: four had had recurrent miscarriages and were treated with progesterone and (in the majority) vitamin E, etc. three going successfully to term. A normal pregnancy in a subject who had not aborted served as a control. In the first patient pregnandiol output was low throughout (10 to 14 mgm during the first 4½ months, and subsequently a maximum of 40 mgm i.e., below Venning's minimum for the same stage) but combined oestrone output was normal. The second woman, a sister of the first, had much higher pregnandiol excretion, and a very notable rise in output of the three oestrogens from the 21st to 24th days may have been related to acute emotional disturbance. The third patient aborted at 22 weeks although her pregnandiol excretion had been sufficiently copious to exclude anxiety concerning the efficacy of treatment (vitamin E 2 or 5 mgm progesterone at three or two days' intervals thyroid and calcium) given from the beginning of the fourth month. The remaining patient showed an extraordinary drop in pregnandiol output at about the sixth month and a lowered excretion throughout pregnancy. In the series neither labour nor abortion was associated with a rise of free oestrogen excretion, there was no clear evidence of cyclical varia-

tions in hormone output at monthly intervals and rhythmic fluctuations in that output occurred towards term in the protracted pregnancies and suggested an extraneous form of control. Hain's second series consisted of over 100 patients in whom the pregnandiol output was measured at intervals of three or four weeks throughout pregnancy, and correlated in some cases with the results of Aschheim-Zondek tests. Cases of threatened abortion numbered 64 among these pregnandiol values were normal in 31 high in 8 and low in 25 i.e. satisfactory in 61 per cent and low in 39 per cent. (In 35 women of this series both pregnandiol analyses and Aschheim-Zondek tests were done. The Aschheim-Zondek test gave a standard or strongly positive result in two thirds and of the 15 cases terminating in abortion, imminent abortion—1 to 20 days—was only once associated with a weak Aschheim-Zondek finding so that symptoms of threatened abortion would not appear to be attributable, even in a majority of patients to low gonadotropin secretion). Abortion occurred both at low and high levels of pregnandiol excretion. 17 cases are recorded in which it followed within 1 to 14 days of a highly satisfactory pregnandiol titre. Hain inclines to the view that vitamin E deficiency may have been a contributory if not a major factor in bringing about abortion. In 12 patients it was not given and in only one case could the dosage be regarded as adequate. Analysing the 14 cases in which abortion took place with a low level of pregnandiol excretion Hain notes that pregnancy had usually been long maintained after the pregnandiol output had greatly diminished taking this into consideration with the fact that amounts of progesterone which should have been adequate to maintain pregnancy often failed to prevent abortion. She regards it as a logical conclusion that progesterone is not the main factor responsible for the maintenance of pregnancy but that abortion occurs independently of the

* "Further Observations on the Role of Progesterone (Pregnandiol) and Oestrogen in Pregnancy. A M Hain *Journ of Endocrinol* Vol III No 1 March 1942

amount of progesterone secreted and is due to a factor, or factors, which progesterone cannot inhibit. Concluding her discussion she writes 'Although it must be borne in mind that the mechanisms of abortion and parturition may be two different things, yet the bearing that these facts have on the causation of parturition is three-fold

(1) A high oestrogen level is of itself insufficient to set in train the events which precipitate labour but may play a secondary part in the process

(2) The values of pregnandiol and oestrogen excreted at the onset of labour (and abortion) are unimportant and may be high or low, there exists apparently, a factor concerned with the control of their elimination and concentration in the body and it is this factor which is probably directly responsible for parturition. This control is cyclic and rhythmic in its effects

(3) There is little doubt that the combined secretion of oestrogen and progesterone is essential for the maintenance of pregnancy, but their utilization may vary from individual to individual and at different stages of pregnancy the peak in the output of both hormones which occurs during the last month of gestation may denote increased secretion or increased elimination or a change in utilization. It may on the other hand indicate that the pituitary responds differently to nervous

stimulation at different stages of pregnancy, or that there is a change in the nature of its nervous control associated with parturition

The time seems to have come when it is neither sufficient nor entirely true to say that parturition is due to a fall in the levels of oestrogen and progesterone and efforts might possibly be concentrated on controlling their secretion and excretion. In this way much might be learnt not only of the cause of parturition but also of the maintenance of pregnancy and the prevention of abortion

The success attending progesterone or vitamin E therapy in cases of habitual and threatened abortion is, without doubt, largely dependent on the cause or causes underlying the condition. In the absence of any means for determining whether this is faulty utilization of progesterone a deficiency of the hormone, vitamin E deficiency or an unspecified abortive factor, it would seem to be safest to combine progesterone and vitamin E therapy of which the latter seems as successful as the former. Clinicians should be cautioned against interpreting a satisfactory pregnandiol output as an infallible indication of a satisfactory pregnancy owing to the number of abortions taking place at such values but be guided by the past obstetric history of the patient. The same applies to positive Aschheim-Zondek and Friedman findings.

W E CROWTHER

Review of Current Literature

Director FREDERICK ROQUES M A , M D M Chir (Cantab) F R C S F R C O G

THIS Review contains the lists of contents and abstracts of the more important articles from the journals with which the *Journal of Obstetrics and Gynaecology of the British Empire* exchanges

The Review of Current Literature has kept the readers of the Journal in touch with current literature throughout the world owing to the war many

journals with which the *Journal of Obstetrics and Gynaecology* previously exchanged are no longer received At the end of the year an Index of all the subjects contained in the articles of the journals reviewed is printed Arrangements are also made to include abstracts of important articles on borderline subjects such as Physiology Biology and Biochemistry

LIST OF ABSTRACTORS

J LYLE CAMERON, F R C S
W E CROWTHER, M B
R H B ADAMSON, M D
B JEAFFRESON, F R C S

P MALPAS F R C S
T N A JEFFCOATE, F R C S
MEAVE KENNY F R C S
JANE H FILSHILL

The Lancet

January 17th, 1942

*Neonatal thrush in a maternity hospital G B Ludlam and J L Henderson

February 7th, 1942

*Peritoneoscopy R Milnes Walker and P Lvon Playfair

March 28th, 1942

*Autodetoxication of stilboestrol during pregnancy Bernard Zondek and Yehuda M Bromberg

May 23rd, 1942

*Blood transfusion for obstetric haemorrhage and shock H L Sheehan

Future of obstetrics (Extract) J M Munro Kerr

June 6th, 1942

Psychology and childbirth (Extract) Ernest Jones

NEONATAL THRUSH IN A MATERNITY HOSPITAL

Ludlam and Henderson state that the high incidence of thrush in the nurseries of many maternity hospitals and its considerable mortality are not sufficiently appreciated Thrush is a specific infection by *monilia albicans* and the authors have made an exhaustive enquiry into its

incidence They collected specimens from the mouth hands and faeces of the infants and from the vaginae and nipples of the mothers Specimens were also obtained from the throats and fingers of the nurses in attendance In their series, 193 infants were swabbed and the fungus was obtained from 70 of them They report that in 1940 the incidence of thrush was 6.4 per cent and in 1939 it was 7.2 per cent In a group of 60 unselected infants swabbings revealed the fungus in 11 cases of these 8 had clinical thrush before they were 10 days old and the remaining 3 developed it after the tenth day Thrush was never seen in an infant from whom a negative swab had been obtained The high incidence of clinical thrush in this small series is due to the fact that very careful inspection was carried out whenever the swab was positive such minute areas of thrush would probably have been missed in ordinary routine inspection Premature babies showed a higher incidence of clinical thrush and of positive swabbings than full time infants

They stress the importance of not diagnosing a white area in the mouth as regurgitated milk curds

or furring of the tongue Milk curds are not adherent and are easily rubbed off Thrush should always be suspected when the tongue has a granular coating The organism can easily be detected by microscopical examination of a fresh scraping teased in a drop of water

Of the possible sources of infection the authors specify the infant's mouth faeces and hands the nurse and the mother From their experiments there was no proof that air-borne infection was an important factor in the spread of thrush Throat swabs of 60 nurses were examined and 20 or 33 per cent gave a positive result They consider that contamination of her hands from her mouth was most likely as these nurses wore masks while handling the infants The higher incidence of thrush in bottle-fed infants could be accounted for by contamination of the feeding utensils Apart from these considerations the authors are of the opinion that the high incidence of thrush is due to overcrowding in the nurseries and the failure to make an early diagnosis with resulting delay in isolation and treatment

PERITONEOSCOPY

Many American authors are writing about the value of direct inspection of the peritoneal cavity through the peritoneoscope In this paper Walker and Playfair give an account of their experience They describe in detail the points in the technique of the operation and how small the discomfort is to the patient Although the organs of the upper abdomen can more clearly be seen they describe how they have been able to inspect the pelvic organs after the patient has been put into the Trendelenburg position This examination is facilitated by an assistant's placing two fingers into the vagina and manipulating the uterus and appendages to enable their different surfaces to be seen

In 16 cases the ovaries were examined 8 on account of menstrual irregularities and 8 for ovarian cysts Multiple unruptured Gräafian follicles and polycystic ovaries were recognized in the former group and 3 cases of peritoneal metastases were seen in the latter group Of 8 cases of carcinoma of the body or cervix of the uterus three showed peritoneal malignant metastases one hepatic metastases and 4 evidence of broad ligament invasion

The authors are of the opinion that in a great

variety of intra-abdominal and pelvic conditions the method helps to settle points of differential diagnosis and that it might well be used more in Great Britain

AUTODETOXICATION OF STILBOESTROL DURING PREGNANCY

The synthetic substance stilboestrol when administered to the human female has all the effects of natural oestrone but certain toxic effects have been noted from time to time These include nausea, vomiting cutaneous and psychic reactions

The authors describe how rapidly oestrogenic hormone disintegrates in the body and that in the rat only one to two per cent of the hormone can be found in the body after a few hours This inactivation takes place partly by combination with glycuronic acid but mostly by enzyme action in the liver The hormone esters are much more slowly absorbed On the other hand stilboestrol is not inactivated by liver tissue to the same degree as oestrone is absorbed slowly like the hormone esters and the absorbed portion is not completely inactivated as 25 per cent of it can be recovered from the urine This recoverable portion is much greater than the usual 1 to 2 per cent of the natural oestrone

Stilboestrol, even when given in very small amounts can give rise to toxic effects in man but the authors found that very large doses can be tolerated during pregnancy They describe the histories of four cases to demonstrate this point In three of them large doses were given to bring about an evacuation of the uterus for special indications and no intolerance was noted In two of these cases a small dose was given a few hours later and marked toxic effects were apparent The fourth case was given large doses of stilboestrol in the first week of the puerperium in order to check lactation and she tolerated this well About eight weeks later a small dose was given and immediately toxic effects occurred The authors maintain that these cases prove that a detoxication of stilboestrol takes place during pregnancy They are investigating the means by which this comes about

BLOOD TRANSFUSION FOR OBSTETRIC HAEMORRHAGE AND SHOCK

As Sheehan points out it is difficult to assess the value of blood transfusion in cases of haemor-

rhage and shock because of the difficulty of obtaining adequate control data a surgeon cannot withhold transfusion from alternate cases in a large series of patients gravely ill from haemorrhage and shock. All that can be done is to compare the mortality from these two causes in a single hospital at a time when few or no transfusions were given with the mortality later when transfusions were being freely given.

From 1929 to 1940, 765 transfusions were given in the Glasgow Royal Maternity Hospital for haemorrhage and shock and 259 women died during parturition as a result of these conditions. The author is of the opinion that obstetric shock is fundamentally the same as shock in surgical trauma and that the value of blood-transfusion for this in obstetrics has a bearing on its value in general. During the first six years of this period few transfusions were given as compared with the second six-year period. During the last three years of this second period there was a decrease in the time taken to get the blood to the patient by the inauguration of a blood bank for the immediate transfusion of the desperately ill patients.

During the second half of this twelve year period there had also been a gradual improvement in obstetric technique, especially in the treatment of placenta praevia. Placenta praevia abortion, post-partum haemorrhage, accidental haemorrhage, rupture of the uterus and inversion of the uterus were the chief obstetric complications which needed blood transfusion for the treatment of haemorrhage and shock. The patients who died were divided into four groups (a) haemorrhage, when the patient literally bled to death before the haemorrhage could be controlled (b) haemorrhage shock, when the bleeding was arrested but the patient died a few hours later with the symptoms of shock, (c) shock-haemorrhage when there was only slight or moderate haemorrhage and the patient died essentially of shock and (d) shock, when the patient died of shock uncomplicated by haemorrhage. The deaths from haemorrhage fell considerably during the twelve year period, those from haemorrhage shock fell moderately, but those from shock haemorrhage and from shock showed no appreciable change.

BRIAN JEAFFRESON

The British Medical Journal

April 4th 1942

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Puerperal cerebral venous thrombosis report of a case J Joseph

Primary thrombosis of cerebral veins in the puerperium report of a case D R Cairns and G Malton

April 11th 1942

Changes in haemoglobin concentration and plasma specific gravity following plasma transfusion J Beattie

Changes in blood volume following transfusions of serum or plasma and the fate of the injected proteins G W Hayward and A Jordan

April 26th, 1942

*Review of the sanitary appliance with a discussion on intra-vaginal packs Mary Barton

May 2nd, 1942

The problem of abdominal pain Francis R Brown

May 9th 1942

*Massive blood loss recovery S Way and F Robertson

May 16th, 1942

*Inhibition of lactation by synthetic oestrogens Josephine Barnes

*Vitamin B₁ in the urine and placenta in toxæmia of pregnancy H C W Nixon, Margaret D Wright and E C Fieller

Hormonal control of lactation Editorial

May 30th, 1942

Sublingual administration of methyl testosterone A W Spence

Full-time abdominal pregnancy with survival of mother and child M L Slotover

The androgens in clinical medicine Editorial

June 6th, 1942

Pregnancy toxæmia and the posterior pituitary Editorial.

June 13th 1942

- *Diabetes mellitus and pregnancy C E Woodrow
- *Paraldehyde in obstetrics Douglas A Mitchell
- Abdominal pregnancy delivery of a living eight months baby Christia F Lucas

June 27th, 1942

- *The expanding pelvis Kathleen Vaughan

July 4th, 1942

- Obstructed labour due to conjoined twins E Ridehalgh
- *Megaloblastic anaemia of pregnancy and the puerperium L S P Davidson L J Davis and James Innes
- *Further data concerning human fertility F Pugh Smith

July 18th 1942

- The incidence of breast-feeding in a small mining town Enid L Hughes
- Nutrition of expectant and nursing mothers report by Special Sub-committee of the People's League of Health

PUERPERAL CEREBRAL THROMBOPHLEBITIS

Cerebral thrombosis in the puerperium may not be primary since emboli may pass from the pelvic veins to the cerebrum by way of the vertebral plexuses. Rise in pressure in the inferior vena cava favours this. The onset of symptoms in recorded cases varies from 4 to 137 days after delivery. The initial headache paraesthesiae and muscular weakness progress to definite paralysis. Death follows epileptiform convulsions and coma. There may be signs of increased intracranial pressure and also of pyrexia. Of 14 cases quoted from the literature and 2 described here 9 ended fatally. To prevent cerebral thrombosis exercises massage and heparin are suggested increase in intra-abdominal pressure by binders and constipation should be avoided. In the presence of cerebral thrombosis, the treatment advised is heparin intravenously, lumbar puncture and intravenous hypertonic solutions to reduce intracranial pressure and avertin or other anaesthetics to control the fits.

REVIEW OF THE SANITARY APPLIANCE WITH A DISCUSSION ON INTRA-VAGINAL PACKS

Women patients between 14 and 50 years of age were questioned and it was found that 95 per cent still use an external appliance during menstruation.

The reasons for this are ignorance of anatomy and fear that intra-vaginal packs may produce sterility or disease. The advantages of a tampon are that it allows freedom of movement and avoids chafing and odour. Moreover it can be changed with a minimum of manipulation of the clothing.

The disadvantages are that virgins may find it difficult to insert and damage to the hymen may be inevitable. Cervicitis and vaginitis might result, but the writer has never seen a case. In discussing the question the author suggests modification in shape size and piston mechanism of the packs which manufacturers might adopt.

MASSIVE BLOOD LOSS RECOVERY

A 4-para, aged 24 was admitted at term with ante-partum haemorrhage. The patient was treated by artificial rupture of the membranes but some hours later she suddenly collapsed. A diagnosis of ruptured uterus was made and a drip blood transfusion was continued for 4 hours. When laparotomy under local anaesthesia was performed 8 pints of blood under pressure were found in the peritoneal cavity and the diagnosis was confirmed. Caesarean hysterectomy was carried out. Four hours later the abdomen was reopened for bleeding from the left uterine artery and seven hours after that a further operation was required for oozing from the cervical stump. The patient had three abdominal operations within 15 hours and was transfused with 11 pints of blood and 1½ pints of plasma. She recovered but her blood group was changed from A to O by the massive transfusions it returned to A by the twelfth day.

INHIBITION OF LACTATION BY SYNTHETIC OESTROGENS

The theoretical basis of oestrogen therapy to suppress lactation is reviewed as is the literature dealing with the use of oestradiol oestrone stilboestrol testosterone propionate and triphenylchloroethylene. In this investigation the values of dienoestrol and hexoestrol were tested and compared with that of stilboestrol. The best results are obtained if treatment is begun as soon as possible after delivery and lactation is more easily suppressed after full-time pregnancies than after abortions.

In the doses used stilboestrol gave the best results but the dose of dienoestrol and hexoestrol

was varied for experimental purposes. Dienoestrol is effective by mouth in a dose ten times less than that required for hexoestrol and stilboestrol. The dose advised for dienoestrol is 2 to 3 mgm over a period of 5 days, and for stilboestrol and hexoestrol 5 mgm twice or three times daily for 2 days followed by gradual reduction over a period of 3 or 4 days. None of the preparations produce toxic effects in the puerperium, and there is little difference in their efficacy.

DIABETES MELLITUS AND PREGNANCY

In spite of modern treatment for diabetes, the mortality to the mother is still 5 per cent, and the foetal mortality is as high as 40 per cent. A case is described to illustrate the management (a) during pregnancy when sugar tolerance tends to vary (b) during labour and the puerperium (c) of the child. Caesarean section at the thirty-sixth or thirty-seventh week is advised and the new-born child should be given dextrose to combat any tendency to hypoglycaemia in the first few days.

VITAMIN B₁ IN THE URINE AND PLACENTA IN TOXAEMIA OF PREGNANCY

Views on the relation between vitamin B₁ deficiency and toxæmia are discussed. Forty-six normal pregnancies and 60 toxæmic pregnancies were investigated. The vitamin was extracted from a 24-hour specimen of urine by absorption, and fed to vitamin B deficient rats. The only patients showing a significant fall in vitamin B₁ excretion were 9 suffering from eclampsia. Fifty-six placentae were examined and again only those obtained from eclamptics were deficient in vitamin B₁. In view of these findings and the similarity in the clinical features of eclampsia and ber-beri it is suggested that vitamin B₁ may be useful in the treatment of eclampsia.

PARALDEHYDE IN OBSTETRICS

Rectal paraldehyde is valuable as an analgesic for primigravidae in labour. Six to 8 drachms in 5 to 6 ounces of olive oil is given when the cervix is 2 to 3 fingers dilated and can be preceded with advantage by omnopon and hyoscine. The disadvantage is that rectal administration gives too slow a result in the difficult patient. Therefore intramuscular injections of 10 c.c. of paraldehyde were

tried and a good result was obtained. This can be supplemented with rectal paraldehyde when labour is prolonged. Paraldehyde is harmless to the patients suffering from toxæmia of pregnancy so intramuscular injections were used in 10 consecutive cases of eclampsia. The effect was satisfactory and all the patients recovered. The child born after the use of paraldehyde is sometimes lazy and sleepy for some hours, but suffers no permanent ill effect.

THE EXPANDING PELVIS

Radiographs of a girl of 14 illustrate the changes which occur in the pelvis on stooping. The pelvis is not a rigid structure but is capable of expansion at the symphysis in front and at the sacro iliac joints behind. This flexibility natural in the very young, can be maintained and developed by well designed exercises even in elderly primigravidae, and can then be used in labour by the judicious use of posture. Perfect ease in parturition necessitates a trained control of muscular contraction and relaxation of the opposing muscles until the co-ordinated movements become instinctive.

MEGALOBlastic ANAEMIA OF PREGNANCY AND THE PUERPERIUM

Sixteen cases of megaloblastic anaemia were investigated. Only 2 were seen before delivery but records of the pregnancies were available. The age incidence is lower than for Addison's pernicious anaemia. It occurs as frequently in primigravidae as in other parity groups. The number of red cells was below 1.7 million in 11 cases and the colour index above 1.0 in 10.

Only 5 cases responded quickly to liver therapy, the refractory cases were given iron, yeast and ascorbic acid in addition. Blood transfusion, often repeated, was required in 12 cases in order to maintain life. Two patients died, the remainder made a complete recovery.

The outstanding features which often distinguish this condition from Addison's pernicious anaemia are the presence of free hydrochloric acid in the stomach, the lower frequency and the degree of macrocytosis and ovalocytosis. Sternal puncture however is essential to make the diagnosis. In every case, except one, examination of the bone marrow showed arrested maturation of megaloblasts.

blasts The name megaloblastic anaemia is therefore, preferable to such terms as pernicious anaemia of pregnancy

The aetiology of this disease is still disputed but the most likely primary cause is a temporary failure of secretion of the intrinsic factor of Castle by the stomach during the later months of pregnancy Other factors may be reduced intake of the extrinsic factor as a result of poor diet, anorexia and vomiting impaired absorption from the intestine, and the demands of the foetus

The condition is often refractory to liver therapy for a considerable time, but most patients ultimately respond and recover completely

FURTHER DATA CONCERNING HUMAN FERTILITY

Data are given showing the variation of 52 consecutive menstrual cycles in the same individual Ovulation is assumed to occur 15 days before the onset of the next period Records of uncontraceptive intercourse during 31 infertile cycles show that there were occasions when intercourse took place as much as 13 days before the beginning of the next period Intercourse which took place on the 9th, 10th, 13th, 14th, 15th and 16th days after the beginning of a cycle was followed by pregnancy

Prediction of the narrower limits of the fertile period can only be made by counting back from the beginning of the next cycle

T N A JEFFCOATE

The Canadian Medical Association Journal

Vol XLVI January, 1942 No 1

*Nutrition in pregnancy J H Ebbs W A Scott
F F Tisdall W J Moyle and M Bell

*The lower uterine segment anatomical changes during pregnancy and labour P J Kearns

*The influence of improved prenatal nutrition upon the infant J H Ebbs, A Brown F F Tisdall W J Moyle and M Bell

NUTRITION IN PREGNANCY

The maternal mortality rate in Canada has fallen from 5.7 to 4.0 per 1,000 live births in the years between 1926 and 1940 The neonatal mortality rate in 1940 was 39 per 1,000 live births, and this was roughly half of the total infant mortality rate Much progress has been made in reducing the infant mortality rate but very little in reducing the neo-natal death rate Study has been made of 229 consecutive deaths in babies occurring before delivery or during delivery or during the first 2 weeks of life Prematurity was the cause of 49 deaths foetal deformity held next place in being the cause of 37 neonatal deaths The ordinary accidents of labour and chronic illness of the mother accounted for the remainder

It is the purpose of this paper to discuss the influence of poor improved or good prenatal diet on the course of pregnancy During pregnancy the daily requirements are total calories 2,400 to 2,800 protein 80 to 100 grams fat 80 to 100 grams carbohydrates 350 to 400 grams calcium 1.5 iron, .020 iodine in iodised salt

Vitamins required are A 6,000 i.u., B₁ 500 to 1,000 i.u., B₂ 3 to 3.5 mgm, C 50 to 75 mgm D, 500 to 1,000 i.u. Expressed as a dietary this would be a daily requirement of 40 ounces of milk 1 ounce of cheese 1 egg butter and meat daily liver once a week a liberal supply of vegetables besides potatoes one orange or grapefruit or 5 ounces of tomato juice Cereals or bread should be given as wholemeal to at least 50 per cent of its amount cod liver oil or its equivalent should be given to the amount of two teaspoonsful

It is found especially among the poorer classes with low incomes that the diet falls far below this standard Frequently this is due to ignorance of the amounts of the different foods which should be taken, or to long established habits In cases of persistent vomiting the food intake is often far below requirements

Prenatal care is now provided by clinics and private physicians for a large proportion of expectant mothers and it is considered desirable that a part time dietitian should be provided to give practical instruction regarding the essentials of nutrition and to help the physician in planning a suitable diet

A study is made of 400 women attending a prenatal clinic A record has been kept of every article consumed by the patient each day for a week This record was then analyzed and the patient concerned placed in one of three groups for observation In group 1 with poor diet there were 120 patients half the patients were left on low diet

as controls. In the second group 90 patients were given extra foods. In the third group were 170 women who had an income sufficient to provide an adequate diet, and who were given advice, this was regarded as a good diet group. There were therefore three groups, on poor, supplemented and good diet respectively, and some interesting tables are presented.

Pre eclampsia occurred in 12.6 poor diet patients, 9.1 in the supplemented group and 7.8 in the good diet group. Threatened miscarriage occurred respectively in the proportions of 11.2, 8.3 and 4.7 per cent, accidental haemorrhage in 3.2, 4.7 and 0 per cent, severe vomiting in 3.4, 1.4 and 1.2 per cent, pyelitis in 5.0, 3.4 and 4.2 per cent, streptococcal vaginitis in 1.7, 0.0 per cent. Freedom from complications were recorded as 30.3, 45.9, and 48.5 per cent respectively in these three groups.

Major complications occurred during labour in these three groups as follows: miscarriages, 6.0, 0 and 1.2 per cent; premature birth, 8.0, 2.2 and 3.0 per cent; stillbirth, 3.4, 0 and 0.6 per cent; primary uterine inertia, 6.0, 0, 3.5 per cent, secondary uterine inertia 3.5, 1.1 and 4.2 per cent. Necessity for blood transfusion, 2.6, 0, and 0.6 per cent.

Figures proportionately comparable were obtained when special conditions were considered such as the average duration of labour, the condition of the mother during convalescence and complications affecting the mother while in hospital. One table is interesting. It gives the average birth weight of the babies: that for poor diet is 7 pounds 10 ounces, supplemented diet 7 pounds 7 ounces and good diet 7 pounds 6 ounces, showing that diet appears to have little or no effect on the weight of the baby. The general condition of the patients 6 weeks after delivery was shown to be poor in the group with low diet, better with the supplemented diet, and good with adequate diet.

Briefly summarized the results of the investigation have shown that there is a much higher incidence of miscarriage, stillbirth, premature birth and other complications in all cases on a poor diet and the whole course of pregnancy appeared to be influenced by supplying an adequate diet when this was already deficient. Numerous highly explanatory tables are included, and a brief biblio-

graphy is appended, together with an excellent resume in French by Jean Saucier.

THE INFLUENCE OF IMPROVED PRE-NATAL NUTRITION UPON THE INFANT

The infant mortality rate in Toronto was reduced by 40 per cent in the years between 1929 and 1939. The decrease in the death rate was 7 per cent for babies under one month, and 37 per cent for infants between one month and one year of age. The same figures held true for the whole of Canada, the infant mortality rate of which in 1937 held sixteenth place in a list of 40 countries. An attempt has been made in this paper to show that the neonatal death rate may be lowered by the provision of a suitable prenatal diet for the mothers.

Three groups of patients were studied from among those attending a prenatal clinic: (a) a group of 120 women on poor diet, (b) a group of 90 women with supplemented diet, and (c) a group of 170 women on good and regulated diet.

The supplemented diet consisted of 30 ounces of milk, 1 egg, and 1 orange daily together with 3½ ounces of canned tomatoes and 1 ounce of cheese. Patients also received a viosterol capsule containing 2,000 units of Vitamin D per day and 2 tablespoonsful of wheat germ per day. This diet was introduced between the fourth and fifth months of pregnancy and continued for 4 weeks after the patient left hospital. The conditions of the mothers were rated either good or bad in the following percentages: those on poor diet, good 66, poor 34; those on supplemented diet, good 94, poor 6; those on good diet, good 85, poor 15. It was also found that the women on poor diet suffered more complications of pregnancy. Anaemia occurred in the following percentages: patients on poor diet, 28.6; supplemented diet, 16.1; good diet, 21.6. Pre-eclampsia and eclampsia, poor diet 12.6; supplemented diet 6.1; good diet, 7.8. Threatened abortion, poor diet, 11.2; supplemented diet 8.3; and good diet 4.7. Miscarriage (in percentages among the three groups as before): 6.0, 0, 1.2; stillbirth, 3.4, 0, 0.6; primary uterine inertia, 6.0, 0, 3.5; premature birth, 8.0, 2.2, 3; pelvic inflammation during convalescence, 9.0, 3.4, 6.1; breast inflammation, 4.5, 2.3, 4.8.

An attempt was made to follow up the babies born to these groups, examinations being made at

intervals of 6 months. The average birth weight of the babies born to the mothers in the poor-diet group was slightly higher than in either of the two other groups, but at 6 months the weight of the babies was greater in those born to the mothers in the supplemented and good diet groups. The ability of the mothers to nurse the babies occurred in the following percentages: In the poor-diet group, 42, supplemented, 52, good diet 49. Breast feeding was regarded as good, fair, or poor according to the capacity of the mother to nourish the child. Poor feeding was noted in the following percentages: Poor diet, 17, supplemented 6, good diet, 8. When all was considered babies of the poor-diet group did not do so well as those on supplemented diet and good diet.

In conclusion it is considered that the percentages of successful pregnancies among poor women was increased by supplying simple foods and the effect upon infant mortality and morbidity was marked.

A short bibliography and reference to previous publications is appended together with a short resume in French by Jean Saucier.

THE LOWER UTERINE SEGMENT: ANATOMICAL CHANGES DURING PREGNANCY AND LABOUR

It was noted by the author on the examination of pathological specimens in the gynaecological and obstetrical museum that there was a relatively high frequency of damage to the lower uterine segment during labour. A study was made in an attempt to correlate the anatomical changes in the lower segment with the incidence of traumatic defects in this region.

Many attempts have been made to delimit the lower uterine segment anatomically, histologically and physiologically, but all are at variance. However it is roughly estimated that the uterus is divided into corpus, isthmus and cervix. The isthmus is approximately 0.5 cm. in length, in the non-pregnant uterus but it is greatly increased in length as the uterus enlarges in hormonal hyperplasia of the myometrium and in the physiological enlargement of early pregnancy.

A lower corpus sphincter is seen in the uteri of almost all mammals or in those developing a corpus luteum, but in those which develop segmental pregnancies such as the pig this sphincter occurs in the caudal zone of each segment or

chamber. This caudal sphincter in the human female develops about the fourth month of intra-uterine life and grows with the uterus. In the full-time foetus it is fully developed and stands in contrast to the small corpus uteri. The isthmus appears to have the same blood-supply as the body of the uterus in the non-pregnant state, but during the first months of pregnancy many new branches arise from the uterine artery giving the lower segment a rich blood supply. The nerve supply of the lower uterine segment remains rather indeterminate. The relative control by the sympathetic and parasympathetic nerves is still disputed by many authorities.

During pregnancy, the isthmic part of the lower uterine segment becomes part of the ovum chamber about the fourth month of gestation, the mucosa not being truly decidualised. Gradually the whole of the isthmus together with the upper part of the cervix, becomes a part of the ovum chamber until at term only the lower third of the cervical canal and external os remain to be dilated during the first stage of labour. In malpositions of the foetus however some of the cervix remains to be dilated thereby causing prolonged labour. During delivery the external os and the remaining portion of the cervix become inextinguishably incorporated in the ovum chamber. The chief function of the internal uterine sphincter in the non-pregnant uterus appears to be the separation of the cervical canal from the corpus uteri thereby separating infections of the cervical canal from the uterine cavity, and it appears to prevent the ovum from falling into and becoming implanted in the cervical canal. It acts as the internal sphincter of the uterus until the third month of pregnancy when it begins to relax. Late in pregnancy it prevents the ovum chamber from becoming over dilated in its lower part and during labour it prevents over distension and possible rupture of the weak isthmic region.

Abnormal function in the lower uterine segment may be due to some aberration of the nerve supply whereby relaxation is replaced by over constriction of the internal sphincter forming what is known as a constriction ring. This ring may be present below the presenting part or may grasp some portion of the foetus. When there is some obstruction to labour, the muscle of the corpus

uteri may become tonically retracted, producing a Bandl's ring, which is drawn high upwards and a new thinned out portion of the uterus develops above the isthmus. This new pathologically-formed segment is much more friable than the physiological lower segment and it is here that rupture usually takes place. Once started these tears may extend far downwards and may result in laceration of the uterine artery or some of its branches.

From the author's findings he has concluded that

a more effectual way of expressing the placenta is to grasp the lower uterine segment and to pull the fundus away from the placenta, instead of pressing the fundus downwards, thereby flattening the lower uterine segment, in the same way firmly packing and distending the lower uterine segment to control uterine haemorrhage will not only produce shock, but will tend further to cause dilatation and increase of the haemorrhage.

Eight excellent specimen illustrations are included in the text.

J. LYLE CAMERON

Medical Journal of Australia

November 15th, 1941

*Endocrine causes of disorders of menstruation and bleeding from the non-gravid uterus. S. Devenish Meares.

November 22nd, 1941

*Special article. Public relations of medical practice. History of events in New Zealand 1941. Maternity benefits.

December 6th, 1941

Pregnancy complicated by a double uterus. Report of two cases. G. Shedden Adam.
Absence of the vagina successfully treated without operation. Kate Campbell.

December 13th, 1941

*Brenner tumours of the ovary, with report of a case. J. D. Hicks.
Erythroblastosis and transfusion accidents in pregnancy.

ENDOCRINE CAUSES OF DISORDERS OF MENSTRUATION AND BLEEDING FROM THE NON GRAVID UTERUS

Meares gives a short résumé of the activity of the endocrine system as it affects the endometrium. He considers that all endocrine treatment should be preceded by accurate physiological diagnosis. He discusses disturbances of sex hormone equilibrium under the following six headings:

1. Menorrhagia and allied uterine bleeding (a) ovular (b) anovular (c) from unproliferated endometrium at puberty or after the menopause, (d) anovular pseudomenstruation.

2. Amenorrhoea.

3. The effects on menstruation of disorders of other endocrine glands (a) thyroid (b) suprarenals (c) pituitary.

4. Granulosa cell tumours.

5. Hydatidiform mole and chorion epithelioma.

6. Dysmenorrhoea.

As regards sex hormone treatment in general he stresses that correct therapy depends upon accurate diagnosis including a proper knowledge of the nature of the deficiency. Haphazard and unscientific treatment with indiscriminate administration of hormones will not prove other than disappointing and may do considerable harm. Sex hormones however administered do not act instantaneously. Even with rapid absorption there is a latent period of 24 to 48 hours. The most harmful effect of oestrogenic therapy is depression of the anterior pituitary function and, so, of ovarian activity. For this reason treatment by oestrogens should never be prolonged more than a few months and is preferably not given continuously to minimise the risk.

He recommends the avoidance of all male hormones. Gonadotropic therapy is not regarded with favour. There is no proof that gonadotropic hormone is followed by a complete ovarian response.

PUBLIC RELATIONS OF MEDICAL PRACTICE. HISTORY OF EVENTS IN NEW ZEALAND 1941. MATERNITY BENEFITS.

There is a special article reviewing the course of events as they affected medical services in New

Zealand since 1935 In 1935 the National party held a departmental committee to consider national health plans

In November 1935 there was a general election and a Labour Government was returned Early in 1936 representatives of the British Medical Association waited on the new Minister of Health offering co-operation and asking for his confidence This request was not acceded to and the Association was kept entirely in the dark until the last minute

In 1936 the Government set up a committee consisting wholly of members of Parliament of the government party The only medical member was a junior practitioner who had just been elected The British Medical Association gave evidence before this committee and later Sir Henry Brackenbury went out to New Zealand to render service both to the Government and the Association In 1938 the Social Security Bill was presented to the House, only after this was it submitted to the Association The Bill became law shortly afterwards

The Social Security Act 1938 had two main objects The first was a system of monetary benefits on a contributory basis and also a system of medical hospital and related benefits The money was to come from a new tax of one shilling in the pound payable by practically the whole community and to replace the previous unemployment tax of eightpence in the pound payable by a smaller circle The medical benefits were to make general practitioners service available to every person in the community Maternity benefits were limited to such services as a general practitioner would ordinarily give

With the next general election matters became very heated and the Bill was used freely in an endeavour to discredit the Labour party It was however, returned to parliament with an absolute majority

In March 1939 the Minister of Health circularised the medical practitioners in an endeavour to obtain their co operation but in the end the medical benefit question was dropped for the time being until 1941

In April 1939 it was announced that a begin

ning would be made with maternity benefits and an offer of contract with the Government was submitted to all practitioners This contract was signed by only 22 practitioners, because conditions were considered to be too irksome both to patients and practitioners, in addition there was no provision for consultant's help There was then prolonged negotiations between the Government and the British Medical Association for several months in the end an agreement was reached This came into effect in November, 1939, and essentially dispensed with any contract of service but allowed the practitioner to fill in a form and for each case of delivery or miscarriage he attended, submit this to the local medical officer of health and receive payment out of the Social Security Fund The usual fee for a confinement is £5 and for a miscarriage £3 In addition there are other fees for abnormal cases on a fixed scale Obstetric specialists under the scheme must be recognized as such by the minister according to standards of academic qualification and mode of practice as laid down by the Health Department Such a specialist may charge a fee in excess of those laid down under social security but no other doctor may do so The general practitioners appear to be fairly well satisfied with the scheme for though the fees are not high there is a certainty of being paid

BRENNER TUMOURS OF THE OVARY WITH REPORT OF A CASE

J D Hicks refers to the 122 recorded cases of Brenner's tumour of the ovary of which the first was observed in 1907

He discusses various theories of its origin and is personally in favour of the view put forward by Meyer that Brenner's tumour is closely related to a large group of serous pseudomucinous papillary adenofibromatous and mixed tumours of the ovary and arises directly from the Walthard inclusions which are themselves derived from the pluripotent coelomic epithelium Clinically they are benign and they tend to occur in elderly patients There is some resemblance to squamous cell carcinoma in some areas and the question of the complete disappearance of the epithelial elements of the tumour is raised

R H B ADAMSON

American Journal of Obstetrics and Gynecology

Vol xli, No 3

Some remarks about maternal mortality in the south J R McCord

*The theca cone and its tropism toward the ovarian surface, a typical feature of growing human and mammalian follicles E O Strassmann

Deep cauterization of the cervix B Z Cashman and J S Frank

THE THECA CONE AND ITS TROPISM TOWARDS THE OVARIAN SURFACE, A TYPICAL FEATURE OF GROWING HUMAN AND MAMMALIAN FOLLICLES

This article is most interesting and stimulating. It has added to our store of knowledge with regard to certain processes in the ovary which have baffled explanation up to the present time. Strassmann describes the four theories which have been in vogue from time to time, concerning the processes leading up to and including ovulation. The first was that of Pfleger who believed that peristalsis of the ovary was the cause of ovulation; this was soon proved to be incorrect as no plain muscle, other than that of the blood-vessels, has ever been demonstrated in that organ. The second theory of ovulation regarded active or passive hyperaemia as the actual cause; this was the result of the current belief that menstruation and ovulation occurred at the same time. A third theory was that enzymes digested the lining of the follicle. The fourth and most popular idea was that ovulation was brought about by an increased pressure within the follicle. The author himself has no doubt that the intra-follicular pressure plays a role in the final rupture of the follicle, but in this paper he establishes the sequence of events which lead to this final stage. The chief question which has to be answered is how do the follicles manage to return to the surface of the ovary.

To elucidate this problem, Strassmann has studied over 18 000 serial sections of ovaries of man, dog, cat, rabbit, horse, cow, and swine over a period of 18 years. He explains the descent of the small follicles into the medulla of the ovary as a passive one, as the cortex offers more resistance to their growth than the stroma; the second movement, the ascent of the large follicles to the surface as an active one which takes place against

the resistance of the cortex. The first step he noticed was that there was an eccentric growth of the theca interna towards the ovarian surface, which showed as a one-sided thickness of the theca interna at the upper hemisphere of the follicle. Where the follicles were near the surface the theca interna at the upper hemisphere was eight to 10 times thicker than at the lower pole. The fibrous theca externa was noticed to be much thicker at the lower pole than at the pole near the surface. So the rapidly-growing theca interna cells at the upper pole had much less resistance of fibrous theca externa to overcome and could more easily expand towards the surface of the ovary. This eccentric growth verified in all the mammalian orders examined as well as in the woman and the author calls it the "theca interna cone". The author maintains that this cone-like growth is an active one towards the surface of the ovary and ploughs a path for the expanding follicle. He also demonstrates a protrusion of a cone of granulosa cells into the theca interna cone so that the axis of the one coincides with the axis of the other. In all the mammals except the horse he found that the theca interna cones grow divergently towards the nearest point of the ovarian surface. In the horse the ovary is covered with meso-ovarium except for one little spot, the ovulatory fossa, from which ovulation takes place. He found that in this animal the theca cones always pointed towards the ovulatory fossa, thus proving that the theca cone had the special function of bringing the follicle up to that part of the ovarian surface where the ovum can enter the peritoneal cavity. He gives his opinion why this theca cone has been missed in an organ which has been thoroughly investigated for many generations. He says that the cone can most easily be recognized when a vertical section has been made through the follicle and that it cannot be seen if, by chance, the section was horizontal. He suggests too, that the recognition of this cone might be used as a more sensitive test of the presence of gonadotropic hormones as the usual ovulation with haemorrhage is a test which needs an overdose of hormone.

BRYAN JEAFFRESON

REPORTS OF SOCIETIES

ROYAL ACADEMY OF MEDICINE IN IRELAND

A meeting of the Section of Obstetrics of the Royal Academy of Medicine in Ireland, was held in the Royal College of Physicians on Friday, March 20th 1942. The President, Dr NINIAN FALKNER was in the chair.

Dr BETHEL SOLOMONS read a paper dealing with SEVEN HUNDRED AND NINETY CASES OF ABDOMINAL HYSTERECTOMY

He showed a coloured film of total hysterectomy. Both the total and the subtotal operations are performed. The indications are given, there are few indications for the vaginal route. It is far more important that the gynaecologist should know when a hysterectomy is indicated than that he should know which variety to do. Both points are important but there are too many unnecessary hysterectomies. Hysterectomy is seldom indicated for such conditions as osteo-arthritis or psychopathic disturbances, but a few examples are described. From answers to the questionnaire it seems of little importance whether the ovaries are conserved or not. The technique of the author was described in *Surgery Gynaecology and Obstetrics* in October 1940. Team work is essential. Methods for the avoidance of pulmonary embolism are suggested. The results of the questionnaire are given. There were 17 deaths in 790 operations: this gives a mortality rate of 2.16 per cent. In at least four of the deaths hysterectomy had been done for extra-uterine conditions so the corrected mortality rate is 1.3 or 1.6 per cent. The details of the deaths are stated. There have been no fatalities from hysterectomy in the practice of the author since 1937. In uncomplicated cases the mortality for hysterectomy should be infinitesimal with improved technique.

Whilst spinal anaesthesia gave wonderful relaxation he thought general anaesthesia was safer, especially in Dublin where the anaesthetists were

so capable. He insisted on team work, and success could not be achieved without a good assistant and skilled nursing both in the operating theatre and in the convalescent period.

The unskilled operator should not attempt either the total or the subtotal operation.

He could not say anything about those patients who had not answered the questionnaire. Only 12 patients in the series complained of urinary symptoms. As a general rule he left a small wick of gauze outside the peritoneum which was brought through the vagina when the total operation was done.

The PRESIDENT in thanking Dr SOLOMONS for his paper said that those present were very fortunate in having had an opportunity of hearing this review of cases of abdominal hysterectomy and of seeing the colour film which had demonstrated Dr Solomon's technique so very well. He asked if this series of cases included cases of hysterectomy which had been done for carcinoma of the cervix. The low incidence of malignant disease in Dr Solomon's cases was remarkable, as was also the fact that there were 12 tuberculous cases. He asked how Dr Solomon interpreted the septic condition of the blood in these cases with regard to the likelihood of thrombosis developing.

PROFESSOR A. H. DAVIDSON said that this was a very important and instructive communication, and the film was an excellent one. He had been very interested in such films for some time and was the first person to show a film at the Obstetrical Section. This film showed Dr Solomon's technique very beautifully. His technique was very good and no criticism could possibly be made of it. It was possible from the film to follow the operation from beginning to end. He asked if Dr Solomon left a drain in the pelvis after total hysterectomy, or if he closed the vagina altogether.

Unless there was definite sepsis in the abdomen he did not think that there was any necessity to leave either a plug of gauze or a drain in. Dr Solomons was to be very highly congratulated on such a wonderful series of cases. To be able to say that in this large series of cases his mortality rate was 2.16 per cent, and that, corrected, it was something less than this was certainly good. He was strongly of opinion however that it was quite wrong for Dr Solomons to be allowed to get away with the fact that in 798 cases he had not found one single case in which vaginal hysterectomy was indicated. This he thought must surely be a misstatement. He would like to contradict it strongly. In his opinion vaginal hysterectomy had a place in obstetrics, and a very definite place. American workers were now coming round to the fact that they preferred vaginal hysterectomy to abdominal hysterectomy in cases in which it could be done, and it could be done fairly often. It was an operation which was practically free from the complication of pulmonary embolism and pleural thrombosis. He thought the reason for this was that the patients were able to move about from the very beginning. Referring to the fact that Dr Solomons had stated that it did not matter whether the ovaries were conserved or not, apart from the psychological effect on the patient, he said that some years ago he had investigated this point. He had found that the menopause occurred earlier, perhaps more severely, in women whose ovaries had been removed. In the last year and a half he had seen four women in hospital who had come back following abdominal hysterectomy complaining of severe pain in the pelvis. In these cases there was cystic degeneration of the ovaries which had been left behind. Quite often when the ovaries were left behind they became cystic. He was inclined not to leave the ovaries at all especially in women over the age of 40 years.

A number of American authorities had recently shown that the incidence of carcinoma of the cervix in cases of retained cervical stump was two or three per cent. He had not done a subtotal hysterectomy for five or six years because he believed that if the cervix was left behind it was very liable to give trouble. His opinion was that total hysterectomy was the operation which should be done and that vaginal hysterectomy should be done as often as possible.

Dr J F CUNNINGHAM said that there was a very big place for vaginal hysterectomy but the cases should be carefully selected. Hysterectomy should in his opinion be done in the way which caused the least danger to the patient. The abdominal route was preferable in the presence of tumours but in other cases the vaginal route should be chosen. Following this operation the patient could move about in bed much more easily and could be allowed to get up earlier. He asked Dr Solomons why he did the subtotal operation so frequently. The complications following this operation were more numerous than those following total hysterectomy. He never closed the vagina. Why did Dr Solomons use the ring which he had shown? Was it to prevent irritation of the skin? This would not occur if dettol was used but it would occur if iodine was used. Why was the spade retractor used if a good anaesthetic was given? Very often there was a certain amount of strain during the operation and this spade retractor would not he thought prevent the intestines from coming down on each side. Even in cases of infection he thought that silk gave a better result than catgut. There was less infection associated with it. He himself always used linen thread. He was interested to see that Dr Solomons used one clamp only he always used several.

Dr R M CORBET said that in doing abdominal hysterectomy he used the technique which he had been taught by Dr Solomons. The spade retractor was of the greatest possible use. It made the operation much easier for the anaesthetist. He would like to support Professor Davidson's plea for vaginal hysterectomy. It was possible to do this operation under local anaesthesia. American obstetricians were very ready to do vaginal hysterectomy but seemed to be very reluctant to do the total operation. This fact might perhaps account for the prevalent prevalence of cervical carcinoma in America. In Ireland the incidence of cervical carcinoma and of stump carcinoma was lower than it was in the U.S.A. He preferred the total to the subtotal operation but he did not always feel that he could do it to the best advantage of the patient. On the whole he had had more trouble following the subtotal than the total operation.

Dr J S QUIN said that the film was excellent and demonstrated very well the technique used by Dr Solomons. He referred to a paper he had recently read on carcinoma of the stump of the cervix following subtotal hysterectomy. In this paper the conclusion reached was that subtotal hysterectomy was never justified. The trouble in most of these cases started six months after the operation. This fact showed that the cervix had not been examined so carefully as it should have been during the operation. There was a considerable amount of bladder irritability following hysterectomy. This irritability was, he thought probably greater after the total than after the subtotal operation. He considered that Dr Solomons had held the mean between the two operations judiciously but he was of opinion that Dr Solomons had put vaginal hysterectomy into a more junior place in the surgical armamentarium than it actually deserved. For a considerable time he had been looking for a case of sciatica caused by a fibroid and he had never found one. He was doing more and more hysterectomies, total and subtotal under spinal anaesthesia and morphia and by this means he had avoided much pulmonary trouble.

Dr J G GALLAGHER suggested that perhaps some of the hysterectomies done by Dr Solomons had been unnecessary. Only 14 operations had been done for malignant disease of the body of the uterus. This fact would tend to point out that most of the operations had been done for relatively simple conditions. About 40 per cent of patients had not replied to the questionnaire which Dr Solomons had sent out. The reason for this might perhaps have been that they were dissatisfied with the operation. If Dr Solomons came across a patient with a large cystocele and a rectocele what did he do? Such cases were he thought suitable for vaginal hysterectomy. Carcinoma of the cervix was a relatively rare condition in Ireland and he did not think that it should be considered in connexion with Dr Solomons's paper.

Dr P FITZGERALD gave some technical advice about the film and suggested that Dr Solomons should use finer silk for sewing up after the operation than he was using at present.

The Master of the National Maternity Hospital said that he had never had an opportunity of

using the spade retractor shown by Dr Solomons. Until about two years ago he had always used packs, and then he had given them up. Now he very seldom had to use one at all, he thought it was an advantage not to use packs. It was his custom not to remove the ovaries if he could avoid doing so. There were times however when it was absolutely necessary to remove them. In the cases in which he had removed them a considerable number of the women had suffered from very severe menopausal symptoms. He would never remove the ovaries unless there were clear indications for doing so.

Dr A P BARRY said that he would never perform total hysterectomy unless it was absolutely indicated as it was an operation which led to the occurrence of bladder symptoms afterwards.

Dr BETHEL SOLOMONS in reply said that cases of cervical carcinoma were not included. He believed that tuberculosis of the uterus was more common than was realized, and the laboratory reported 12 in the series. In some of these hysterectomy had been performed for tuberculosis of the Fallopian tubes. If an operation could be deferred until the sedimentation rate was slow infection was less likely and thrombosis less probable. He pointed out that the title of his paper was 'Abdominal Hysterectomy'. He had done vaginal hysterectomy but it should be reserved for those cases in which vaginal repair was necessary in addition to the removal of the uterus. He found with his technique that there was less shock after the abdominal operation and he preferred that route to the vaginal. In the series there were 352 subtotal operations and 438 total.

In recent years he had been more inclined to perform the total operation but there was no danger of malignant disease in the stump after the subtotal operation if great care were taken in the selection of cases in which the cervix was absolutely clean. If the ovaries were cystic he removed them. He found it easier to work when the clamps were removed and suturing done before the uterus was taken away. Silk was preferable to catgut unless infection was present he used fine silk. There were only two cases in the series in which intractable sciatica had been cured by the removal of large tumours.

Dr J F CUNNINGHAM PROFESSOR J McGRATH,
and Dr D K O'DONOVAN read a paper on

POSTPARTUM PITUITARY NECROSIS ILLUSTRATED
BY GRAPHS SHOWN ON THE SCREEN

Details of the obstetrical histories of three cases of postpartum pituitary necrosis are presented. These cases represent the varying degrees of severity with which the disease may manifest itself. One patient died soon after parturition, a second survived in a condition of chronic invalidism, while a third was in relatively good general health 18 months after the onset. The post-mortem on the fatal case showed a large area of necrosis in the anterior lobe of the pituitary.

The necessity for immediate recognition and treatment during the first week is stressed. Large amounts of carbohydrate given by every possible route are essential in the acute phase when complicated by hypoglycaemia. The diagnostic value of the response to small subcutaneous doses of insulin is exemplified. The intravenous insulin test of Russell and Fraser (1941) as a diagnostic procedure is confirmed. Using these insulin sensitivity tests the value of desoxycorticosterone, cortin and pituitary adrenocorticotrophin as substitution therapy was assessed. None of these hormones established a normal insulin sensitivity. The adrenocorticotrophin (cortrophin of Organon Ltd) caused a significant increase of body weight, alleviated the myasthenia and anorexia. It is therefore considered a useful but incomplete, source of substitution therapy.

The various hormonal deficiencies which constitute Simmond's disease are outlined and it is assumed that the human pituitary secretes a hormone which directly influences metabolism, besides the indirect effects mediated through the adrenal cortex and thyroid.

Professor W J JESSOP in thanking the authors for this extremely interesting and instructive paper said that he would like to pay a special tribute of admiration to Dr O'Donovan for the magnificent analysis which he had given demonstrating the way in which the deficiency of the various hormones was responsible for various symptoms. He referred to the sensitivity of patients and said that it was really necessary to know how much anterior pituitary a person needed. At the present time in England some surgeons were trying to cure Cushing's disease by putting radon seeds into the neighbourhood of the sella turcica.

PROFESSOR BIGGART referred to three cases of acute necrosis which had proved fatal, and three cases of Simmond's disease which had been proved at post-mortem examination. In the rat 33½ per cent was sufficient to retain metabolism as regards the pituitary. In an examination of 2 000 pituitaries which he had carried out he had found only three cases of necrosis. It would be of great interest to know exactly how these cases were produced. It was possible that the retention of the placenta might play a more important part than shock. An attempt should be made to see if there was an increase in the circulating hormones of placental origin. The only other condition in which necrosis was found was cavernous sinus thrombosis.

Dr P FITZGERALD said that the peculiarities of the anterior pituitary were well known. These peculiarities were not present in the posterior lobe but were confined to the anterior. He asked Dr O'Donovan if any sign of thrombosis had extended into the hypothalamic region in the present cases.

Dr CUNNINGHAM and PROFESSOR McGRATH replied and the meeting concluded.

THE
Journal of Obstetrics & Gynaecology
of the British Empire

VOL. 50, No 2

NEW SERIES

APRIL, 1943

EDITORIAL

THE EDITOR desires to call the special attention of readers to the reproduction of a post card reproduced on the reverse of this page received from a British prisoner of war

It is the desire of the Editor and the Directors to send the Journal free of cost to all prisoners of war, from any and all of the Allied Nations, in all parts of the world to whom it would be acceptable and useful. We accordingly beg our readers to assist us by sending to the Editor, c/o Messrs Sherratt & Hughes, The Old Boys' School, Poplar Grove, Sale, Cheshire, England, particulars of the address and exact description of any prisoners of war known to them, such names will be at once placed upon our list of subscribers for the duration of the war period

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Sir, Please accept my heartfelt
wishes for the success of
1941. It makes one realize that at last our
professions, and the even the most difficult part
is to conduct the interview and the interview. The
one to all the who are with us for

Yours

King



The Present Position of Antenatal Care in Obstetrics *

BY

J D GREEN, B A ,
Radcliffe Infirmary, Oxford

HISTORICAL NOTE

THE modern system of antenatal care is a product of the last half-century, but the study of hygiene of pregnancy is much older. Certainly this study was in existence in Egyptian times, and the work of Engelmann¹ suggests that still earlier evidence of it is to be found in the habits of primitive tribes.

At the time of the Grecian civilization the foundations of the knowledge of the anatomy of pregnancy were laid by the discovery of a number of presentations and positions, and the study of obstetrics flourished in the Near-East and also in India. All this was swept away in the Moham-medan tide and lost to mankind.

With the Renaissance, the man-midwife made a tentative reappearance and the art of obstetrics gained a new lease of life. Vesalius' "*De Corpore Humano*" marks the beginning of the new era and the birth of a scientific knowledge of the human pelvis. In England, in 1542, Raynald,² who was something of a plagiarist, published "*The Byrth of Mankynde*". This book is a transcription based on another work by Roesslin (this is hinted in the preface) and indirectly is a descendant of the writings of Soranus of Ephesus. It is more conservative than might be expected, the filthy nostrums of contemporary pharmacopoeas are not to be found in it. In discussing the

hygiene of pregnancy it covers an unexpectedly wide field, even including a reference to psychology —

"Also the Mydwife muste enstruct and comfort the partie, not onlye refreshing her with goode meate and drinke but also with sweete wordes geuyng her good hope of a speedefull deliveraunce, encouraging and enstomacking her to patience and toleraunce."

The textbooks of Mauriceau³ and Smellie⁴ discuss the disorders of pregnancy in some detail, but no records exist of Institutions for pregnant women before the 18th century. Ténon⁵ described the "*Hôtel Dieu*" in 1788, and in 1789 the "*Secret Maternity*" was founded in Prague. Beds for expectant mothers were often attached to Parisian obstetrical clinics, but too often were reserved for healthy young women who could make themselves useful by doing house-work. Various "refuges" for unmarried mothers were established during the nineteenth century, notably in Paris and Edinburgh, and some doubtless undertook a certain amount of medical treatment, but it was not until 1901, when Ballantyne's⁶ famous address was published, that the profession properly appreciated the needs of pregnant women. Ballantyne's work, and the fine contribution of the Boston midwives are too well known to require comment. These mark the introduction of the modern antenatal clinic and of the concept of the prematernity hospital.

* Based on an essay awarded the Radcliffe Clinical Prize University of Oxford (open to medical students in their second year of clinical training)

AIMS AND EXPECTATIONS

The aims of antenatal care are a normal pregnancy, a safe and natural labour, and a healthy child. Their achievement depends on the early recognition and treatment of any abnormality of the pregnancy or inter-current disease, and the application of measures to relieve anxiety or discomfort.

Following the introduction of antenatal clinics and the provision of proper hospital accommodation for women with diseases of pregnancy, a decline in the maternal mortality-rate was expected. Up to 1936 no such fall had occurred and many papers have been written to explain the "failure" of antenatal care.

CRITERIA OF THE VALUE OF ANTENATAL SUPERVISION

Maternal mortality is not the only possible criterion of the value of antenatal care. Ballantyne expected the "prematernity hospital" to lower the neonatal and stillbirth death-rates. Stillbirths became notifiable in 1927 and, per unit population, the stillbirth rate has declined steadily since then (0.70 in 1928, 0.59 in 1939 and, provisionally, 0.55 in 1940). This decline, however, is not due to antenatal care but to the falling birth-rate: the number of stillbirths per 1,000 births has remained almost constant. The neonatal death-rate has fallen steadily during the present century, but the fall is, in the main, due to causes other than antenatal care: the decreased incidence of summer diarrhoea, for example.

The value of the reassurance and education which mothers receive at clinics cannot be assessed. It seems, therefore, that the maternal mortality-rate is the best gauge of the value of antenatal care, though, with due caution, Raynald's words, made in another connexion, may again be quoted:

"these tokens, although they have a certain reason and appearance yet, be they not always infallible but only likely."

SOME GENERAL FACTORS INFLUENCING MATERNAL MORTALITY

Antenatal care is not the only factor influencing the maternal mortality-rate, before judging the effect of antenatal care on the maternal death-rate it is necessary to conjecture what would have happened to that rate if clinics did not exist and if the patients with the diseases of pregnancy were still considered suitable for general wards.

Since 1900 the female mortality-rate for England and Wales has fallen to half its previous level. A similar fall in the maternal mortality-rate might have been expected but has not materialized. On the other hand many changes have taken place in the social and economic conditions of women in the same period. More women live in towns, more women are employed in industry and there may be a tendency to have children later in life.

A clear difference between rural and urban maternal death-rates is not demonstrable in this country,⁸ but is seen in some American statistics. More recently Dorn⁹ has shown that even this may be due to the American system of classifying deaths to places of occurrence and not to places of residence.

The 1937 White Paper of Maternal Mortality⁸ showed that there was a high maternal death-rate associated with certain trades (e.g. spinning and weaving) if, in general, trade exerts but a small influence. The effect of economic conditions will be referred to later.

THE "FAILURE" OF ANTENATAL CARE

Some of the reasons advanced for the "failure" of antenatal care are that

- 1 Only a proportion of maternal deaths are preventable by antepartum care
- 2 The falling fertility-rate has led to an increase in the proportion of relatively dangerous first pregnancies

3 There may be a tendency for women to have their children at a later and consequently more hazardous age

4 Intrapartum care may not be of high standard and there is tendency towards unnecessary interference

5 The services for the provision of antenatal care are inadequate

Each of these points will be taken up in turn

I PREVENTABLE DEATHS

Browne¹⁰ suggests that relatively little can be done by antenatal care for deaths which follow a normal labour or deaths which are due to sepsis, haemorrhage or shock (including ectopic gestations and abortions)

The Departmental Committee of 1930-1932 on Maternal Mortality and Morbidity¹¹ attempted to assess the "primary avoidable factor" in individual deaths by laying down definite standards for obstetrical care. Until war broke out the Chief Medical Officer of Health¹² reported on a similar investigation every year. Table I is taken from this information and similar sources.

This table shows some of the estimates which have been made of deaths prevent-

able by antenatal care, and indicates that a fair reduction in the maternal death-rate should be possible.

2 AGE and 3 THE INCREASING PROPORTION OF PRIMIPAROUS BIRTHS

In the past less emphasis has been placed on the tendency for women to have children later in life than on the effect of the falling fertility-rate. Clearly the two questions are linked because on the whole multiparae are older than primiparae, but most statistical investigations either fail to distinguish between the two problems or fail to make it clear that one and not the other is under consideration. Yerushalmy¹³ gives the "puerperal fatality-rates" for different ages and different orders of pregnancy in New York State.

His information shows that for primiparous births, the "puerperal fatality-rate" is more than half as high again for women between 25 and 29 as compared with mothers under 20 in first pregnancies. Although the mean age of marriage has not altered significantly since 1861, birth-control measures and modern conditions may

TABLE I

Authority	Year	Deaths with full report	Deaths preventable by antenatal care			
			Preventable deaths (With full report)		(With full report)	
			Number	Per cent	Number	Per cent
Munro Kerr and MacLennan ²⁶	1932	466	333	70.8	165 (a)	35.4
Departmental Committee ¹¹	1932	3432	1576	45.9	526 (a)	15.3
Chief Medical Officer of Health ¹²	1935	1210	827	68.3	388 (a)	32.1
	1936	1404	889	63.3	341 (a)	24.3
"	1937	1107	717	64.8	293 (a)	26.5
	1938	1252	622	49.7	294 (a)	23.5
White Paper ⁸	1937	770	—	—	443 (b)	57.5
Douglas and McKinlay ¹⁶	1935	2465	1447	58.2	694	28.2

(a) Deaths with primary avoidable factor

(b) Deaths which might have been influenced

TABLE II
Puerperal Fatality rate (per 10,000 "total deliveries")

Order of birth	Under 20	20 to 24	25 to 29	30 to 34	35 to 39	40 and over	Total
1	16.8	21.4	27.2	57.1	95.3	174.3	28.2
2	11.0	12.0	20.1	31.1	36.3	31.3	19.8
3	—	5.5	23.3	20.7	24.8	44.8	18.5
4 and 5	—	18.4	15.6	22.7	51.4	96.8	29.5
6 and 7	—	—	33.7	24.1	43.8	78.4	37.9
8 and over	—	—	48.1	42.5	59.3	62.9	55.1
2 and over	9.5	11.0	21.3	26.5	44.4	69.5	25.9

From Yerushalmy *et al* *Public Health Reports* 1940 11 1195

well be tending to make women older at their first confinement

Statisticians agree^{13 14 15 16 17} that while the risk of first pregnancies is high relative to the second and third, "high order" pregnancies are much more dangerous. An increase in the proportion of primiparous births is certainly taking place (Stocks¹⁷ Yerushalmy¹³), but at the same time a decrease in the numbers of *Grandes Multiparae*, who run a much greater risk, is occurring.

Munro Kerr,¹⁵ Greenwood and Stevenson¹⁸ and Stocks seem to agree that the falling fertility-rate has not exerted a great influence on the trend of maternal deaths. Stocks says "the falling fertility-rate may be held responsible for increases in the maternal mortality-rates in England and Wales as a whole amounting to round about 1 per cent and not more." It cannot be argued that the high maternal death-rate in women who have had many children is due to large families in poor homes, for both

TABLE III
Social Status and Maternal Mortality

Cause number (International classification)	Cause	Status of husband				All married women
		1 & 2	3	4	5	
140 to 150	All causes	4.44	4.11	4.16	3.89	4.13
142 to 150	Causes other than abortion	3.94	3.55	3.60	3.32	3.58
142 to 143	Ectopics and 'other accidents of pregnancy'	0.17	0.15	0.16	0.12	0.15
144	Puerperal haemorrhage	0.50	0.44	0.48	0.60	0.49
145	Puerperal sepsis	1.45	1.33	1.21	1.16	1.29
149	'Other accidents of childbirth'	0.52	0.42	0.46	0.40	0.44
146, 147	Toxaemias	0.81	0.81	0.85	0.68	0.79
148	Phlegmasia alba dolens	0.40	0.30	0.32	0.26	0.31

Class 1	Professional etc
2	Intermediate
3	Skilled artisans
4	Intermediate
5	Unskilled labourers

Status of husband
(From 1937 White Paper)

here and in America (1937 White Paper⁸, Goddard and Palmer¹⁹) it has been found that the poor have a better chance of surviving pregnancy than the rich (Table III) Economic depressions do, however, appear to affect the maternal mortality-rate adversely²⁰

credits and cloak their ignorances" "they use pothooks, pack needles, silver spoons, thatchers hooks and knives to show their imagined skill"

The Registrar General's tables of the mortality associated with Caesarean section show that these deaths are steadily increas-

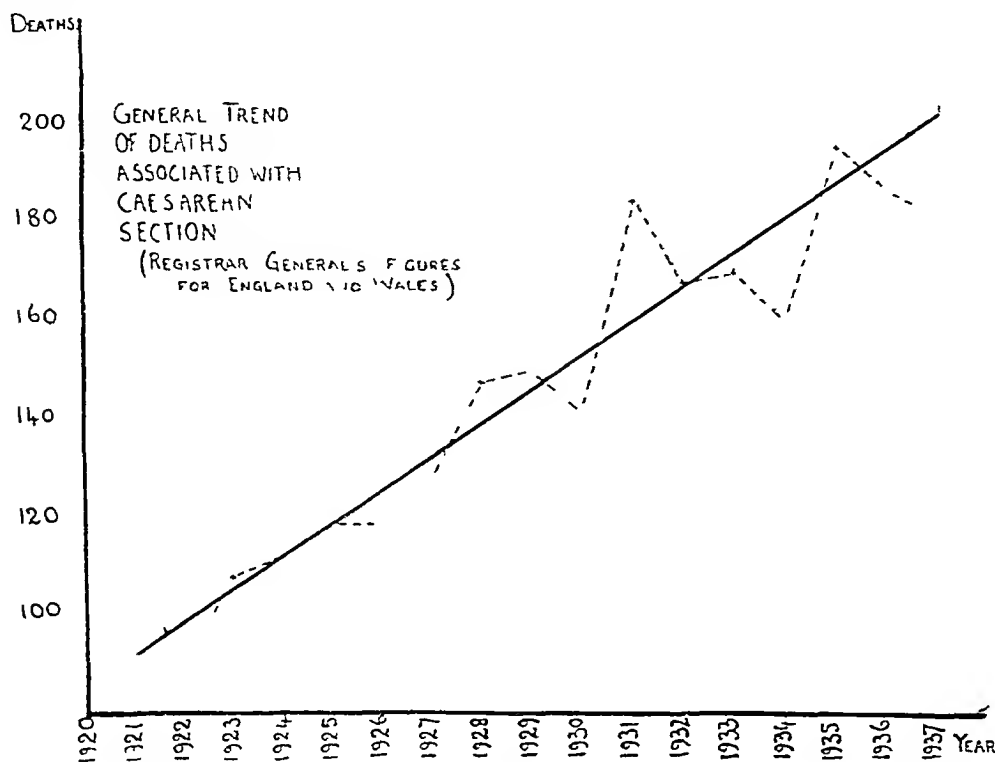


FIG 1

4 INCREASING TENDENCY TO UNNECESSARY INTERFERENCE

The danger of interfering with the course of nature has long been recognized William Harvey²¹ refers to—

'The younger more giddy and officious midwives who mightily bestirre themselves and provoke the expulsive faculty and who persuading poor women to their three-legged stool before the time do weary them out and bring them in danger of their lives

While Willughby²¹ says

'They will leave nothing undone to save their

ing (Fig 1) Though the latest figures are not available, the trend of deaths in previous years suggests that about twice as many occur annually now as 20 years ago The operation is no longer a last resort in women desperately ill, indeed there is now an unfortunate tendency to use it for trivial reasons Certainly there is no evidence that the mortality-rate has increased rather the reverse It can be assumed, therefore, that considerably more than twice as many of these operations are performed annually at the present time as were performed 20 years

ago As Browne has pointed out, such figures are misleading in that interference is often a life-saving measure, in other words, the patients who die are now said to die "from operation" whereas formerly the cause of death would be given as "obstructed labour" or whatever the indication for interference was. Nevertheless the fact of an increasing tendency to interfere can-

death-rate from puerperal sepsis. The Registrar General's figures show no such increase and, since 1936, there has been a significant decline in the death-rate from puerperal sepsis running parallel to and practically accounting for the similar decline in maternal mortality (Fig 2). Statistical calculation shows that the chances that this decline is due to an error of sampling

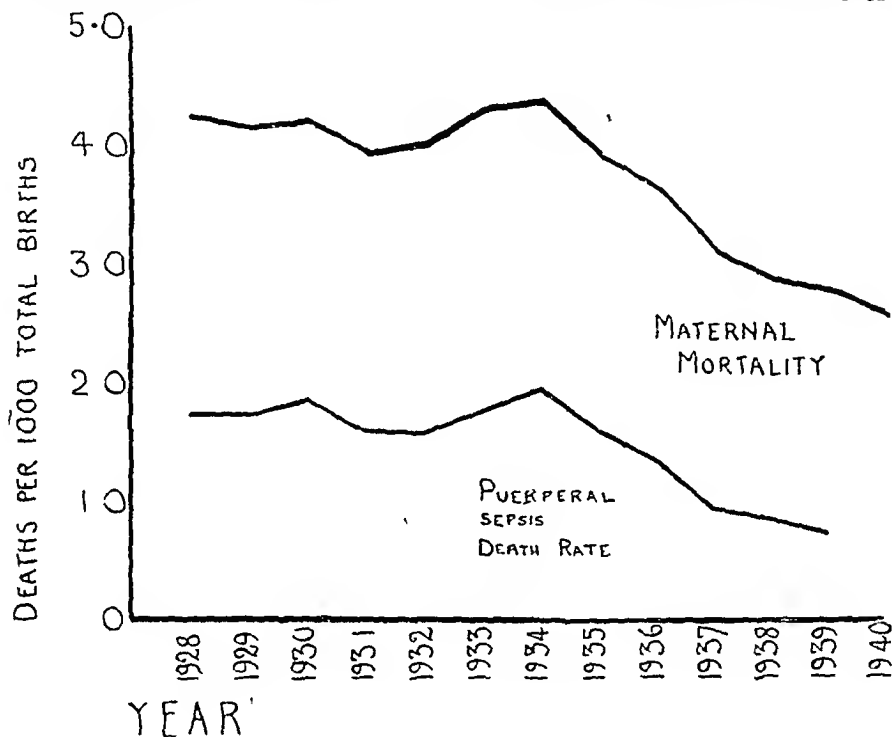


FIG. 2.

not be denied. What we want to know is how much of the interference is unnecessary and dangerous?

Goddard and Palmer¹⁹ found that women who were well-to-do not only had a higher maternal death-rate than those on relief, but also experienced two or three times the amount of operative interference.

Every laceration of skin or mucous membrane is a potential nidus of infection, and the increasing use of operative procedures might be expected to lead to an increasing

are more than 1,000 to 1 against. Several factors are, no doubt, responsible, the most important of which are probably the improvement in technique of delivery, especially the general adoption of face masks in hospitals and private practice, and the introduction of sulphonamide therapy, which latter coincides exactly with the beginning of the decline. A possible decline in the virulence of streptococci must be considered. The passing of the Midwives Act of 1936 may also have a

bearing on the matter It cannot be said that antenatal care has been responsible in any way It is, however, conceivable that it played a part in the United States, where a fall in the maternal death-rate began as long ago as 1929

It an increasing rate of interference is leading to a rise in the maternal death-rate and if no increase has occurred in the puerperal sepsis component it might be expected that the number of deaths from some component other than sepsis would have risen, such as deaths from placenta praevia or accidents of childbirth for example Except for sepsis and possibly toxæmias each fraction of the maternal death-rate has shown a remarkable constancy Improved technique and advances in the treatment thus appear to counterbalance with surprising exactness whatever bad effect excessive interference is having In passing, it may be suggested that the peculiar steadiness of almost all components of the maternal mortality-rate implies that some general factor is exerting a malign influence on the mother's chance of surviving pregnancy What this may be can only be conjectured it may be connected with some change in the habits of women or to an increase in the number of confinements in unsatisfactory institutions

In America interference may play a more serious part Some American statistics show a high death-rate from accidents of childbirth,²⁰ and some States with a high maternal mortality-rate show a high rate of interference²²

* It is likely that a recent slight decline in deaths from causes other than sepsis is to be accounted for by the fact that though these deaths are not *primarily* due to sepsis yet sepsis is not infrequently a contributing factor Improvement in the prophylaxis and treatment of sepsis is likely to show its effect in many other categories of the maternal mortality-rate

The influence of the increasing use of anaesthesia is more difficult to evaluate, nor can its influence be separated from that of operative interference While a certain risk is attached to the use of every anaesthetic, there are occasions when it is dangerous to withhold anaesthesia, notably in eclampsia Chloroform, a dangerous anaesthetic, is rather widely used on the doubtful supposition that it is safe in pregnancy and child-bearing

5 INADEQUACY OF ANTENATAL CARE

The responsibility for the care of the expectant mother lies both with her attendant and with herself The White Paper of 1937 stated that the responsibility for attending women antenatally was distributed as follows —

Medical Officers at Municipal Antenatal Clinics	14 per cent
Midwives and members of Hospital or Institution staffs	30 „
General Practitioners	56 „

The attendance at clinics and the number of clinics available have risen steadily in the past few years Table IV shows some figures which have been collected from the Chief Medical Officer of Health's Reports

It should be noted that "attendance" does not mean *adequate* attendance, for a single visit is classified as "attendance" Many women attend infrequently and many too late, and figures of attendance, therefore, give a flattering picture of the real situation It may be seen that responsibility for antenatal care lies in the main with the private practitioner Often he has not had any post-graduate experience of obstetrics and he may not have sufficient time to fulfil his duties adequately The doctor who attends privately does not always have the facilities for following the course of his patient's pregnancy, she may cease to attend or omit to call him in Further, he

TABLE IV

Year	Clinics			Percentage of pregnant women in attendance
	Provided by local authority	Voluntary	Total	
1930	860	189	1049	27.3
1931	995	198	1193	33.9
1932	1060	217	1277	38.9
1933	1090	250	1340	42.2
1934	1130	266	1496	43.07
1935	—	—	—	48.48
1936	1279	289	1568	48.85
1937	1307	285	1592	54.19
1938	1389	287	1676	60.58

TABLE V
Deaths of Booked Cases in Various Hospitals

Hospital	Years	Booked cases	Deaths	Death-rate per 1000
A	1927-30	8088	23	2.80
B	1928-31	6140	10	1.60
C	1927	2347	6	2.50
D	1927-30	6004	4	0.66
E	1928-29	2002	2	1.00
F	1927-30	7891	29	3.70
G	1927-30	6774	16	2.30
H	1926, 1929, 1930	4238	61	14.40
I	1925, 1927, 1928, 1929, 1930	3442	32	9.30

(Browne F J *Lancet* 1932 ii 1)

may be unable to see her at or after her delivery. In well-run antenatal clinics medical attendants have these facilities and are thus clearly at an advantage.* In 1932 Browne¹⁰ said "It would probably be true to say that not more than half of the preg-

* On the other hand some statistics show that with meagre facilities for antenatal care, excellent results are obtainable by private doctors. In N. Dakota, which claims the lowest maternal mortality-rate in the U.S.A. 92 per cent of the confinements are conducted by private practitioners (Moore²³).

nant women in this country yet receive any antenatal care and that it cannot be regarded as adequate in more than 10 per cent. Since then it appears that attendances at clinics have doubled. If we assume that 25 per cent of women now receive adequate antenatal care and that roughly one-third of all maternal deaths are preventable antepartum by due care, then this amount of care by itself could not be expected to account for a reduction in the maternal mortality-rate of more than 10 per cent. Only a little more than the year to year "scatter" prior to 1936. The fact that there is a good deal

of variation between the maternal death-rate of different hospitals (Browne) suggests something at fault in those in which it is very high, but the fault is not necessarily in the antenatal care, the high death-rate is often dependent on the type of case admitted

It appears that in a good Maternity Home a woman is less likely to die from puerperal sepsis than on the district. The Departmental Committee of 1932 dealing with normal cases, found that the death-rate from puerperal sepsis in three large hos-

in this type of institution is responsible for a general adverse trend in the maternal mortality-rate and is tending to keep that rate constant in spite of all advances in the art of obstetrics. Where a good Maternity Home is available, however, it seems to be the place of choice for a confinement. A number of such institutions have the very low maternal death-rate of 10 per 1,000 live births or even less. In strictly comparable cases, the evidence that antenatal care is of value is very strong. Munro Kerr gives data for "booked" and "unbooked"

TABLE VI

The Effect of Antenatal Care on Various Conditions in the Royal Maternity Hospital Glasgow

(Collected from Munro Kerr's 'Maternal Mortality and Morbidity' Edinburgh, 1933)

Condition	Total cases	Booked		Unbooked	
		Cases	Per cent mortality	Cases	Per cent mortality
Hyperemesis	390	109	2.75	281	10.3
Albuminuria Pre-eclamptic toxaemia and nephritic toxaemia	1208	642	2.18	566	7.9
Eclampsia	392	55	7.27	337	16.3
All above toxaemias	1990	806	2.60	1188	10.8
Placenta praevia	419	70	4.28	349	13.4
Accidental haemorrhage	514	93	3.20	451	6.6
Abortion	3453	653	0.30	2800	1.03
Occipito-posterior	635	272	0.30	363	2.20
Face or brow	112	30	—	82	6.10
Breech	936	330	1.80	606	3.60
Transverse	153	40	—	113	5.30
Contracted pelvis generally (not including slight deformities)	1428	823	2.70	605	4.40

pitals was only half that prevailing on their respective midwives' services. In many Institutions, however, the results are far less favourable. Colebrook²¹ emphasizes the dangers of proximity between surgical and obstetrical patients, especially in small nursing homes. It may be that a large increase in the proportion of women delivered

in a number of conditions and these show marked improvement in the death-rates of all disorders investigated. While this does not entirely eliminate the error due to the moribund emergency case, which finds inclusion in the "unbooked" category, it does provide evidence that this is not the only factor responsible for a lower

mortality in the "booked" Kerr found that about 10 per cent of patients who died were moribund on admission

Kinloch, Smith and Stephen²⁵ used another approach. They found that the difference in mortality between "booked" and "unbooked" patients was small ("booked" 5.4 per 1,000 live births, "unbooked" 6.9), but when patients who came to the clinic because of definite symptoms were excluded, the mortality in the "booked" patients fell to 3.8 per 1,000 live births.

In conclusion, mention must be made of the most disappointing of all aspects of antenatal care—the failure to control the death-rate from toxæmia. Munro Kerr calls eclampsia "this eminently preventable disease" and yet deaths from toxæmia are as frequent as ever. There may be an increased tendency for toxæmia masked by the effect of counter measures. If this is not so then it must be presumed that, on the whole, patients receive inadequate attention. This may be because they fail to attend often or early enough at the clinic, or because the early signs of the disease are missed when the woman is examined. Moreover, examples are not lacking of women correctly diagnosed as suffering from toxæmia being unable to obtain the necessary treatment because of lack of local facilities. Selected statistics of "booked" patients show very low death-rates from the toxæmias of pregnancy, but the high death-rate in the country as a whole remains as a challenge to the medical profession.

SUMMARY

Some aspects of the influence of antenatal care on the maternal mortality-rate have been discussed with reference to current literature. It is suggested that

1. Antenatal care is not yet in the right hands and, at the same time, facilities for the treatment of conditions already diagnosed are not always available.

2. In spite of the rapid increase in the number of clinics and in the numbers of attendances, available evidence suggests that only a minority of women yet receive adequate antenatal care.

3. The facilities already in existence cannot be expected to exert a large effect on the maternal mortality-rate.

4. The fact that there is remarkably little year to year variation in any component of the maternal mortality-rate except sepsis, in spite of improvements in obstetrics, suggests that a general adverse factor is influencing all maternal deaths. This factor may have something to do with a change in the habits of women—a tendency for first confinements to occur late in life, for example—or may be due to a widespread tendency to be confined in unsatisfactory institutions.

ACKNOWLEDGMENTS

I should like to express my special gratitude to Professor J. Chassar Moir for his encouragement and help and for a few additions to the text, to the Editor of this Journal for many helpful corrections, criticisms and suggestions, and to Dr D. W. Taylor of the Ministry of Health, for recent statistical information.

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An Investigation of the Effect of Ergot Alkaloids in Promoting Involution of the Postpartum Uterus

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INTRODUCTORY NOTE

ERGOT of rye administered by mouth stimulates uterine contraction. This fact was known as far back as 1582 when Lonicus¹ recorded (freely translating from early German) "In the ears of rye or corn, long, black, hard, narrow cones are found these corn-cones are regarded by women as a special remedy, and a reliable medicine for inducing the labour-pain of the mothers if three are taken several times by mouth." The use of ergot by the medical profession dates from 1808 when the New York Medical Repository published a letter by Dr John Stearns² in which he praised the value of a decoction of ergot powder for hastening lingering parturition. Following this lead, the medical profession quickly accepted the new drug, using it sometimes wisely, but often dangerously, as contemporary writings show. Before long the "pulvis ad partum" was re-named the "pulvis ad mortem" it had become evident that the "incessant and urgent" uterine contractions stimulated by incautious use of the drug could lead to foetal asphyxia or even to rupture of the uterus. These were bitter experiences, but the lesson was well learned, and at the present day

ergot is not given in normal cases till after expulsion of the foetus

THE CLINICALLY ACTIVE ERGOT ALKALOIDS

In view of matters to be later discussed it is necessary to give a short description of some of the active principles of ergot. Because of its remarkable pharmacological effect, ergot was one of the first drugs to claim the attention of the modern chemist. Analytical investigation has yielded results so rich and varied that ergot can be said to have proved a treasure-trove to pharmacology. Besides the alkaloids to be presently described, substances so different, for example, as histamine, tyramine, acetylcholine, and the sterols—including vitamin D—can all trace lineage to ergot. The wealth of physiological knowledge that mention of these names brings to mind is some indication of the rich fields for research that are sometimes uncovered by investigations primarily directed to an entirely different end. Certain of the above substances stimulate the uterus, but do so only when injected into the muscle or blood-stream they will not be further discussed.

Turning to matters of immediate concern,

5 alkaloids have been isolated, all of which bring about a pronounced contraction of uterine muscle. Each of these alkaloids is accompanied by an inert isomer, and, in addition, no less than 14 molecular complexes have been described.³ Fortunately for clinicians the active alkaloids can be simply arranged. There is, on the one hand, the group represented by ergotoxine and ergotamine. These alkaloids are very sparingly soluble in water, are slow to act, especially if administered by mouth, but, once absorbed, are rather persistent in effect. If given in excess, they produce various toxic symptoms, notably the peripheral gangrene which characterizes chronic ergot poisoning. Standing in sharp contrast is ergometrine. This alkaloid is readily soluble in water, is remarkably quick in action even if given by mouth, and is non-toxic in dosage greatly exceeding that used in clinical practice.

Ergotoxine was isolated and described by Barger and Dale in 1906; it is now generally sold as the ethanesulphonate. At an early date Dale accidentally discovered that the alkaloid also had a remarkable property of nullifying or even reversing the effect of sympathetic stimulation. Physiologists were thus given an invaluable tool by which many involved physiological problems have since been unravelled. In 1918 ergotamine was isolated by Stoll. This alkaloid is very similar in chemical composition to ergotoxine and is indistinguishable from it in biological effect.^{4, 5} Ergotamine is usually prepared in the form of a tartrate, and is marketed under the trade names of Gynergen and Femergin. Other members of this group, more recently isolated, have not come into clinical use.

In 1932 Moir⁶ showed that crude extracts of ergot had an action on the puerperal uterus which could not be explained by any of the then-known constituents. This unknown principle had a quick and characteristic action when given by mouth and there was every reason to suppose that it was the agent responsible for the traditional clinical use of the drug. After considerable chemical investigation and clinical trial the new principle

was isolated by the late H. W. Dndley and found to be an alkaloid with certain unusual characteristics. The name ergometrine was given and the announcement of the discovery in 1935 included a description of the chemistry and method of preparation of the new alkaloid.^{7, 8} Meanwhile work proceeding in at least three other centres led to the almost simultaneous announcement of the isolation of substances with similar clinical action but not in all cases it seemed, with similar chemical characteristics. Later each of these principles was found to be identical with ergometrine.⁹ Some confusion was caused by the number of names thus introduced by the workers concerned and by the various commercial firms manufacturing the drug. The following may be mentioned—Ergometrine, ergotocin, ergotrate, ergostetrine, ergocline, ergobasin.¹⁰ In this country, and in Europe generally, there has never been any question of patent or commercial rights in the preparation of ergometrine and the name originally given by the discoverers continues to be used. In the U.S.A. the Council of Pharmacy of the American Medical Association recommended the adoption of the name ergonovine.

These alkaloids have the effect of stimulating powerful contractions in the uterus at term or during the puerperium. At first, the contractions are of short duration ($\frac{1}{2}$ –1 minute) but follow each other in such rapid succession that the uterus as a whole has no time to relax, so that a state of spasm prevails. Later, as the effect diminishes, individual strong contractions alternate with intervals of relaxation.

There are two main uses of ergot in obstetrics. One is to stimulate uterine activity in cases of postpartum haemorrhage, the other is to promote—so it is supposed—the involution of the postpartum organ. Elsewhere one of us has discussed in detail the modern use of ergot preparations.^{11, 12, 13} For the first indication, the value of the drug has been amply proved, for the second indication, uncertainty regarding its usefulness still prevails. The present paper presents fresh observations on the rate of involution

of the postpartum uterus and the possible influence of repeated ergot administration

THE MEASUREMENT OF THE INVOLUTION OF THE UTERUS

Some years ago (1936 and 1937) patients delivered at the British Postgraduate Medical School (Hammersmith Hospital) were divided into 3 groups in order to determine whether ergot therapy would influence the

ergometrine, 92 patients had been given ergotamine, and 359 had been used as controls. From each case-record the height of the uterine fundus above the symphysis pubis on the 2nd, 4th, 6th and 8th days was noted, and the arithmetical means for the 3 groups of patients obtained (Chart 1). The standard deviations in all twelve sub-groups lay between 0.6 inches and 0.8 inches.

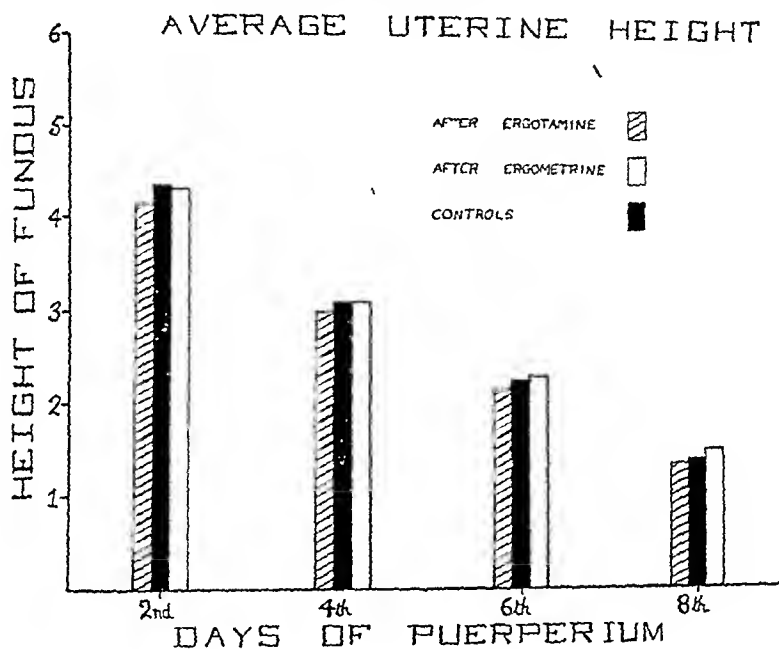


CHART 1

Diagram comparing at two-day intervals the average uterine height in the three groups of cases investigated at the British Postgraduate School

involution of the uterus. The patients in the 1st group were given ergometrine 0.5 mg by mouth 3 times daily for the 1st week of the puerperium. Those in the 2nd group received ergotamine (femergin) 1 mg 3 times daily by mouth for a similar period, and those in the 3rd group were observed as controls. One of us (C.S.R.) studied the notes of 600 such patients, of these 589 were found suitable for analysis. One hundred and thirty-eight patients had been given

By subtraction, the average involution of the uterus in successive 2-day intervals was obtained, and Table I was prepared, this shows that the difference between corresponding figures in the 3 groups never exceeded $\frac{1}{10}$ of an inch.

These findings were of considerable interest, they were, however, open to the serious criticism that the measurements had not been made by one observer throughout. It was, therefore, decided that further and

more accurate measurements should be made. This latter investigation was made in the Radcliffe Infirmary, Oxford

that either the bladder or rectum had not been emptied, the patient was considered unsuitable, and the readings discarded

TABLE I

Involution of the Uterus in Inches

	2nd to 4th day	4th to 6th day	6th to 8th day
Controls	1.2	0.9	0.8
Cases receiving ergometrine	1.2	0.9	0.8
Cases receiving ergotamine (femergin)	1.2	0.8	0.8

METHOD

Normal puerperal patients were chosen, and divided into 3 groups. The women in the 1st group received 1 tablet (0.5 mg) of ergometrine thrice daily, those in the 2nd group were given one tablet (1 mg) of ergotamine tartrate (femergin) thrice daily, the patients in the 3rd group were used as controls. In the earlier trials the drugs had been continued for 7 days, this period was now reduced to 3 days in order to fall in line with the work of other investigators to be discussed later. The observations were continued for 8 or 9 days.

On the 2nd, 4th, 6th and 8th mornings following delivery, at approximately the same time, one of us (C.S.R.) measured the height of the uterine fundus above the symphysis pubis. To ensure, as far as possible, that the bladder and rectum were empty each patient had received special preparation. On the 2nd morning an enema was given and the height of the uterus measured immediately after the bowel and bladder had been emptied. On the 3rd night an aperient was given, followed by a further enema next morning unless the bowel had already been satisfactorily emptied. The bladder was again emptied immediately before the uterus was measured. The same preparations were made before the 3rd measurement. If there was any suspicion

Trial measurements were made before any readings were recorded so that the nursing staff might become accustomed to the routine of preparation. Satisfactory observations were made in 78 cases. It was found that accurate measurement was best obtained by marking the skin at points corresponding to the highest point of the fundus of the uterus, and the upper border of the symphysis pubis, and then measuring between the marks with a pair of engineer's calipers.

DIFFICULTIES

Four difficulties quickly became apparent. The first 3 pertained to the measurements, the last to the condition of the bowel and bladder.

1 It is impossible to measure the height of the uterus above the symphysis pubis more accurately than to the nearest $\frac{1}{4}$ inch, to obtain even this precision a thin subject is necessary. In some cases the uncertainty amounts to nearly 1 inch.

2 The uterus can be moved downwards or upwards in the abdomen, sometimes by as much as 1 inch.

3 Towards the end of the 1st week of the puerperium the uterus, in some cases, tilts backwards, it is then more difficult to measure its height than it was in the early days of the puerperium.

4 It is not always possible to be certain that the bowel and bladder have been completely emptied however carefully the patient has been prepared

A good example of the last-mentioned difficulty is illustrated in Chart II which

limited by minor variations in the state of the bowel and bladder

When these 4 difficulties are taken into consideration, the estimated experimental error in each measurement, even when the greatest care is observed, is at least $\frac{1}{2}$ inch

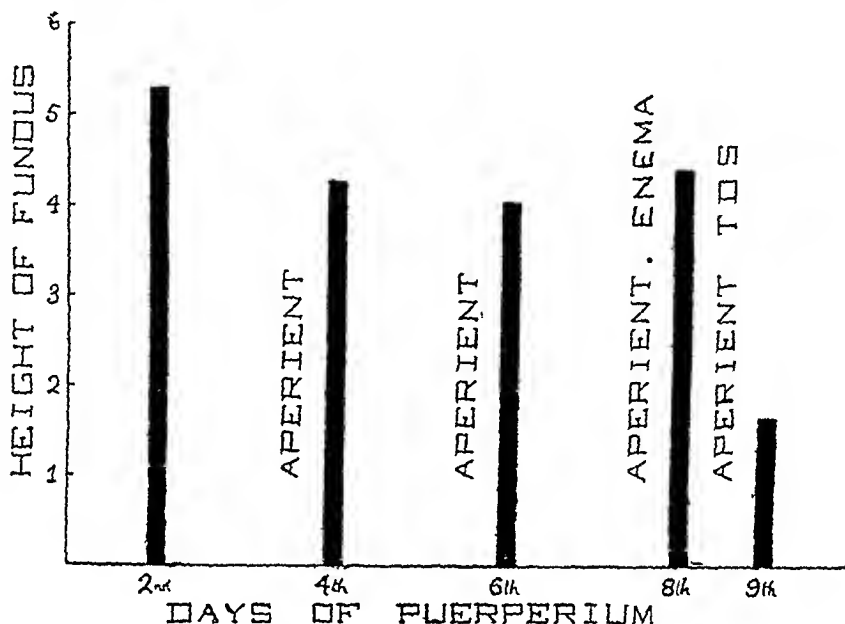


CHART 2

Diagram illustrating how a full rectum may apparently interfere with normal uterine involution

shows the distortion of the uterine involution curve by the varying fullness of the rectum. It will be seen that on the 8th day the fundus was higher than on the 6th day despite the fact that the patient had received an aperient the night before, and an enema administered shortly before the measurement was made. Cascara extract, thrice daily was then prescribed, and the bowels freely opened. Subsequent readings show that the uterus had "involved" 3 inches in one day. As already stated, cases showing erratic readings such as these were not considered suitable for analysis. While such a degree of inconstancy was rare, it is certain that precision of measurement is always

THE RESULTS OF MEASUREMENTS OF INVOLUTION

The average height of the uterus in the 2nd, 4th and 6th days in the 3 groups was obtained and Chart III prepared. This shows that the average height of the fundus of patients receiving ergotamine or ergometrine is slightly higher than in the control series, though the rate of involution in the 3 groups is similar.

Attention must now be directed to another factor which alters the apparent size of the puerperal uterus. During contraction the uterine outline is better defined, and the organ tends to push itself forwards against

the abdominal wall. The outline is altered, and the height may appear to be greater than it is when the uterus is measured in a relaxed state. Bearing this in mind, it is improbable that the slight difference in recorded height has any significance.

Consecutive normal cases were again divided into 3 groups. The patients in the 1st group were used as controls, the 2nd group received ergometrine 0.5 mg thrice daily by mouth for the first 3 days of the puerperium, and those in the 3rd group

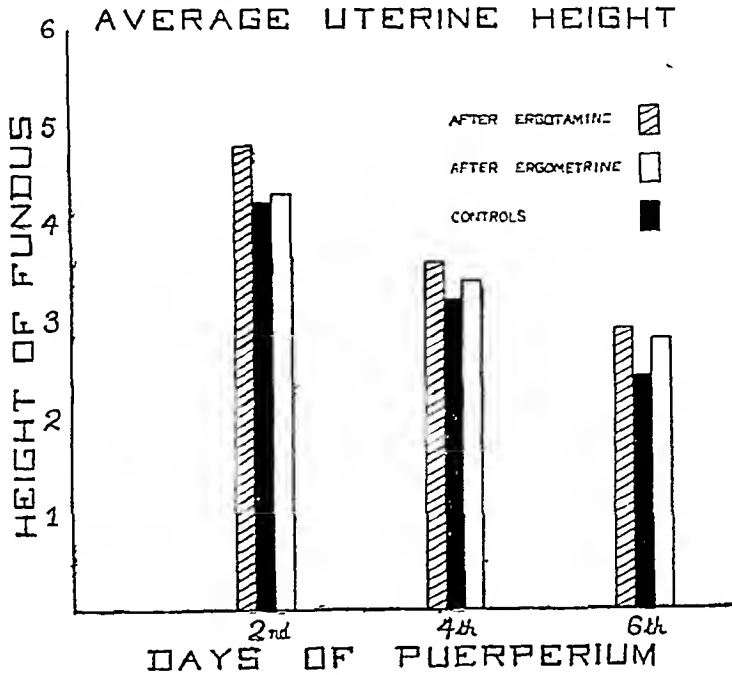


CHART 3

Diagram comparing at two day intervals the average uterine height in the three groups of cases measured with special precautions at the Radcliffe Infirmary Oxford

These observations, therefore, do not give any support to the usual belief that ergot, administered over a period of days, hastens uterine involution.

THE EFFECT OF ERGOT ADMINISTRATION ON THE AMOUNT AND CHARACTER OF THE LOCHIA

The effect of ergometrine and of ergotamine on the amount and character of the lochia was also studied by one of us (C S R).

received ergotamine (femergin) 1 mg thrice daily by mouth for a corresponding period. All discarded sanitary pads were placed by the nurses in special bowls and examined personally at approximately the same hour each morning. Just over a 100 cases were recorded, the patients being more or less evenly divided into the 3 groups.

It was soon discovered that some women after childbirth hardly soil the sanitary pads they wear, most of the lochia escaping when a bed-pan is used for the

purpose of emptying the bowel or bladder. Examination of the pads alone may thus give an entirely false impression of the amount of lochia passed. The co-operation of the nursing staff was, therefore, obtained, and each time a bed-pan was used an entry was made on a special chart recording whether the lochial discharge was absent, scanty (small clots), moderate (medium clots), or profuse (large clots). While this arrangement had the disadvantage that the charts were filled by different observers each day, it was a decided improvement on the methods employed in any previous investigation of which we have knowledge. From the pads personally inspected and the special charts kept by the nursing staff a reasonably reliable record of the amount and character of the lochia passed during the previous 24 hours was obtained.

lochia in all 3 groups was red and profuse in practically every case. Comparisons between the 3 groups made on the 4th, 6th, 8th and 9th days did not show any constant change. Comparisons made later than the 9th day were unsatisfactory as so many of the patients were then ambulatory (Table II).

In view of the above difficulties, only guarded conclusions can be drawn from this investigation.

1 The normal variation in the quantity and character of the lochia is very great.

2 The practical difficulties in collecting all the discharge and in estimating its amount are so numerous that unless wide variation is constantly observed, records of lochial discharge do not give any trustworthy indication of the effect of drugs on the uterus.

TABLE II

Character of Lochia

	4th day of puerperium			6th day of puerperium			8th day of puerperium			9th day of puerperium		
	E	C	F	E	C	F	E	C	F	E	C	F
Profuse lochia	10	20	11	9	11	3	4	7	9	3	4	4
Moderate lochia	24	14	17	21	23	27	26	24	18	15	22	18
Scanty lochia	1	1	2	2	2	0	3	2	3	6	5	2
Totals	35	35	30	32	36	30	33	33	30	24	31	24

E—Ergometrine

C—Controls

F—Ergotamine

As in the case of the uterine measurements, several difficulties were encountered. A patient might show a heavy loss on a single occasion, but on all others the discharge might be scanty. Colour was also an unreliable guide: a free loss might be brown in colour while a smaller loss might be bright red. For these and other reasons a completely satisfactory basis for measurement could not be found.

The following observations were made. For the first 3 days of the puerperium the

3 Administration of ergometrine did not produce any constant change in character or quantity of the lochia.

4 Administration of ergotamine (femernin) did not produce any constant change in character or quantity of the lochia.

THE PUBLISHED RESULTS OF OTHER WORKERS

From time to time observations have been recorded purporting to support the long-

held view that ergot administration promotes uterine involution. Certain recent papers will now be briefly considered and criticisms offered.

In 1935 Der Brucke¹⁴ compared the uterine involution in 171 consecutive women who had been divided into 3 groups. To the 1st ergotamine (gynergen, femergin) was given, to the 2nd fluid extract of ergot, the 3rd group was used as a control series. Mention is not made of the difficulties of measuring the height of the uterus, or whether precautions were taken to ensure an empty bowel and bladder before each examination. The statement is made "administration of ergot or its alkaloid, ergotamine tartrate, during the first 3 days of the puerperium hastened involution," but later modified "our series is too small to warrant definite conclusions." The published graphs show that the average involution rates in the 3 groups are practically identical. The slight variation recorded can be readily explained by reasons already given.

In 1936 Davis, Adair and Pearl¹⁵ compared uterine involution in a series of 200 patients treated with ergonovine (ergometrine) with the involution of a short control series, and concluded "The group of patients that received ergot in the form of ergonovine exhibited a more rapid decrease in the size of the uterus." This statement is based on the evidence of sketches showing the outline of the involuting uterus determined by abdominal palpation. One illustration, depicting the uterus on the 1st, 4th, 7th and 10th days, represents the average of 200 sketches made for each of these days; those patients had received 0.2-0.4 mg of ergonovine maleate thrice daily for the first 3 days of the puerperium. This picture of the average involution of treated cases is contrasted with a series of sketches showing the involution of the uterus in 7 individual control cases. As might be expected, considerable variation is seen in the

behaviour of the "controls", thus in one case the uterus on the 7th day still rises $\frac{3}{4}$ of the distance from the pubes to the umbilicus, while in another it rises only $\frac{1}{3}$ of that distance. It is stated that measurements were made when the bladder was empty, but there is no indication that the other obstacles to accurate measurement were overcome. In some of the control cases involution is quicker, in others slower, than the average of the ergonovine series. It is difficult from the evidence presented to draw any certain conclusion regarding the influence of ergot therapy.

It is further stated that pyrexia (defined as "any patient who exhibited a temperature of 38°C (100.4°F) or over, on any day after the first 24 hours") was encountered less often among the treated cases. The incidence was 37 in the ergot group of 200 cases, compared with 53 in a group of 200 untreated patients. When these figures are subjected to statistical analysis,* it is found that the difference is not significant though nearly so. In view of this trend we were prompted to examine our own records from the point of view of the morbidity-rate. An analysis was made according to the Ministry of Health standard of morbidity ("any febrile condition occurring in a woman within 21 days after childbirth or miscarriage in which a temperature of 100.4°F (38°C) or more has been sustained during a period of 24 hours or has recurred during that period"). The results were as follows. In the untreated group, 14 in 360 cases, in the ergometrine group, 5 in 138 cases, in the ergotamine cases, 1 in 92 cases. Statistical analysis shows that

* With Yates' correction for continuity, χ^2 gives a value of 3.2 corresponding to a probability between 0.5 and 0.1. Therefore the morbidity figure rates in the two groups do not vary by more than can reasonably be attributed to chance.

these figures are within the limit of expected chance variation

In 1938 Kushner and Wahrsinger¹⁶ compared the involution of the uterus following a single dose, given immediately after delivery, of four proprietary preparations of ergometrine. It is highly improbable that a single dose of the quick-acting ergot alkaloid could have any prolonged influence on uterine involution, and it is not surprising to find that the published graphs do not show any significant difference in the involution-rate of the five groups. Indeed, the investigation forms an interesting demonstration of the chance-variation that is ever present in observations of this nature. On the evidence presented we are unable to agree that the administration of the drugs influenced involution, even less can we accept the writers' contention that a superiority can be ascribed to this or that commercial preparation of the new ergot alkaloid.

In 1940, Lounsbury¹⁷ compared the involution of the uterus in patients who had been given ergonovine (ergometrine) thrice daily for the first 3 days of the puerperium with a control series that had received only 1 single dose of ergonovine (ergometrine) immediately after the delivery of the placenta. Daily measurements of the height of the fundus and the amount and character of the lochia were all recorded. Mention, however, is not made of how the measurements were made, or what precautions, if any, were taken to ensure that the rectum was empty before the fundus was measured, nor is there indication that the difficulties of obtaining an accurate estimation of the amount of lochia passed each day, have been appreciated. In the first graph, the average difference between the two groups is about half a centimetre. One of the charts shows a completely irregular curve, on the 2nd, 4th, 6th and 8th days the uterus was higher in the abdomen than on the 1st, 3rd, 5th and 7th days. As the result of our ex-

periments we have no hesitation in stating that the cause of these variations is to be found in the varying state of the bladder and rectum, it certainly does not indicate a delayed or irregular uterine involution. Involution is a continuous physiological process and nothing short of another pregnancy will reverse it. Lounsbury states that with the ergot treatment there was a decrease in the amount of lochia. He records that up to 59 per cent of all his cases in both groups had scanty lochia up to the 3rd postpartum day, not one of his cases had profuse lochia on the first postpartum day. Now, in our own cases, we found that it was an almost invariable rule that the lochia was profuse, whatever the treatment, until the 3rd postpartum day. We are therefore unable to understand the criteria by which the character and amount of lochia were judged, and cannot make useful comment on the observations recorded.

In all the foregoing examples we believe that the claims made have not been substantiated. In no case does it appear that the difficulties of the investigation have been fully appreciated, nor is there evidence of adequate safeguard against the inclusion of fallacious recordings.

DISCUSSION

THE NATURE OF INVOLUTION

Involution of the uterus following childbirth is a unique process. The endometrium is quickly repaired and the myometrium rapidly shrinks to a small fraction of its previous size. There is good reason for believing that the hypertrophy during pregnancy, and the later rapid diminution of size is mainly governed by the level of oestrogenic hormone in the blood stream.¹⁸ That such rapid changes should take place leaving an organ capable of undergoing the changes of future pregnancies is an indication that the process is a physiological

phenomenon rather than a simple disuse atrophy. With these facts in mind, it is reasonable to suppose that an unimpeded blood supply will favour involution. Indeed, a powerful and sustained contraction may be harmful. After Caesarean section the uterus is often seen to be tightly contracted with a wrinkled and blanched surface. Bleeding from the cavity is reduced to a minimum because the blood-flow through the uterine blood vessels has been stopped or, at least, greatly lessened, by contraction of the interlacing muscle-fibres—the so-called “living ligatures” of the uterus. Were it possible for this extreme contraction to be long maintained the uterus might well undergo a necrosis just as if real ligatures had been placed on the blood vessels supplying the organ. This, however, does not happen. Before long the initial contraction is followed by alternate contractions and relaxations, and as the puerperium advances, the periods of relative inactivity are prolonged, so that the natural flow of blood through the organ is fully restored.

If at any stage of the puerperium activity is forced on the uterus, the steady involution of that organ may well be hindered, for an active muscle does not atrophy. It has previously been explained that the ergot alkaloids bring about a series of contractions so rapid that the uterus as a whole has no time to relax. Each muscle-fibre, is, however, performing many times its previous amount of work. It is a mistake to suppose—as is sometimes done—that ergot causes the uterus to become firm in an inactive or static sense. Uterine muscle is not leather in a tanner's vat; it is living tissue, and a “firming” is the result of greatly increased work of muscle-fibres. The “nice hard uterus” of the ergot-treated patient is not necessarily a well-involuted uterus, and comparisons between treated and untreated women are

valid only when the organ in each case is in a similar state of activity or rest.

THE USE OF ERGOT IN CASES OF UTERINE INFECTION

Those who prescribe a course of ergot to patients suffering from puerperal uterine infection do so in the twofold belief that the drug will check any tendency to sub-involution, and that it will expel infected material from the uterine cavity. The first of these suppositions has already been discussed, the second will now be considered. In patients presenting symptoms of uterine sepsis, pathogenic organisms are living and multiplying in the uterine wall, and mere contraction of the organ will not get rid of them. Violent activity may, on the contrary, disseminate infection. It is a cardinal rule that all inflamed organs should be kept at rest, and if this is the correct treatment for, say, a septic finger, it is difficult to understand why matters should be reversed for a septic uterus. Further, if by the uterine contraction the blood supply is appreciably reduced there will also be a diminution of the supply of white-blood cells, of natural anti-bodies, and, on occasion, of chemotherapeutic substances. Ergot therapy may thus have a harmful influence.

Although we cannot find any sound basis for prescribing a course of ergot for the treatment of puerperal sepsis, special mention must be made of a retention of lochia in the uterus. A small quantity of dark blood—15 or 20 c m—is often contained in the uterine cavity, this can scarcely be regarded as abnormal. On rare occasions, however, a sharply ante- or retro-flexed corpus uteri may compress the cervical canal at the level of the internal os and lead to the accumulation of a considerable quantity of lochia. In these circumstances, an increase of uterine activity may overcome the hindrance to the lochial discharge,

although, on occasion, a catheter must also be passed in order to ensure efficient drainage. Such cases are rare, and we cannot, therefore, produce figures bearing on the effects of therapy, it seems reasonable, however, to make use of a single full dose of ergot in the treatment of this specific abnormality. If evacuation of retained lochia is observed, the dose may be repeated at discretion. This procedure is quite distinct from the routine, repeated administration of ergot to promote involution or to treat uterine sepsis—practices for which we can find no justification.

CONCLUSION

The long-held belief that continued administration of ergot favourably influences the course of uterine involution receives no support from the investigations reported in this paper. The practice of giving the drug throughout the puerperium appears to arise from an imperfect understanding of the nature of uterine involution on the one hand, and of the mode of action of ergot on the other. There is little doubt that vast quantities of this drug are daily used for purposes that may fairly be described as wasteful, useless, and possibly even harmful. At this time of national stress, importation of ergot is difficult and uncertain, there is, therefore, urgent need to conserve the existing supplies of this essential drug.

ACKNOWLEDGMENTS

The earlier part of this investigation was made at the British Postgraduate Medical School (Hammersmith Hospital) and we gladly acknowledge the help of Professor

James Young and of the L C C Hospital organization. Among the later cases were some under the charge of Mr J A Stallworthy to whom our thanks are also due. We also wish to record our appreciation of the help given by the nursing staffs of the Radcliffe Infirmary and of the Hammersmith Hospital.

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Further Bacteriological Studies of Severe *Clostridium Welchii* Infections following Abortion

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IN Melbourne one of the greatest problems in connexion with abortional infections is that of the fulminating types due to *Clostridium Welchii*. At the Women's Hospital it is not uncommon for there to be as many as 12 deaths in one year from such infections.

In 1939 a special study of these cases was commenced. The first stage of the work showed that *Cl. Welchii* was often present in the vagina, in the uterine contents, in the urine and even in the blood without causing symptoms of a severe infection. It was, therefore, clear that the mere isolation of *Cl. Welchii* from the tissues or body fluids of the patient was of little diagnostic significance so far as severe infections were concerned. It was also shown that the strains of *Cl. Welchii* causing the severe infections differed from most of the strains obtained from patients who did not develop symptoms of a severe infection due to *Cl. Welchii*, both in regard to growth characteristics and the amount of capsular material produced in broth (Butler ¹).

The problem of the rapid bacteriological diagnosis of the severe *Cl. Welchii* infections was largely solved by the examination of smears from the cervical canal. In cases of severe infection cervical smears showed heavily capsulated bacilli and considerable destruction of the leucocytes. This combination was not seen in the smears from

patients who, although infected with *Cl. Welchii*, did not show the symptoms of a severe infection (Butler ²).

These findings suggested that the severe *Cl. Welchii* infections associated with abortion were caused by only certain variants of this organism. It is the purpose of this paper to set forth the evidence that has so far been obtained in support of this contention.

MATERIAL STUDIED

More than 600 strains of *Cl. Welchii* recently isolated from abortional cases were studied in regard to one or more of the following —

- 1 Growth characteristics
- 2 Capsulation in broth cultures
- 3 Production of α toxin
- 4 Phagocytosis by human leucocytes
- 5 Pathogenicity of washed cultures for guinea pigs

In addition, smears from the cervical canal were examined in 80 cases in which there was a proven *Cl. Welchii* infection. All of the above methods showed that the strains of *Cl. Welchii* were subject to great variation.

In order to determine the significance of these variations, the strains causing the severe infections were compared with those isolated from cases without symptoms of a severe *Cl. Welchii* infection.

* Working with a grant from the National Health and Medical Research Council of Australia

The strains associated with the severe infections were divided into two groups according to whether the patient's outstanding symptom was jaundice, which was usually accompanied by haemoglobinaemia and haemoglobinuria, or whether the patient's condition was characterized by collapse without jaundice. Both these clinically recognizable types of Cl. *Welchii* infection were distinguished by the rapidity with which the infection became generalized. In 26 cases in which the attempt to cultivate from the blood was made before treatment was instituted, Cl. *Welchii* was obtained in all but 3, and in 15 of these cases the patient's first symptom of infection of any kind developed less than 18 hours prior to taking the blood. Further, in some of these cases Cl. *Welchii* was detected in the blood immediately after the appearance of the first symptom characteristic of Cl. *Welchii* infection. It seems probable that the symptoms recognized as typical of a severe Cl. *Welchii* infection occur only after the infecting organism has invaded the blood stream.

The strains isolated from abortifol cases without symptoms of a severe Cl. *Welchii* infection were regarded as the control group. Two groups of cases were particularly important. Firstly, those patients in whom Cl. *Welchii* was shown to multiply in the uterine contents but in which the infection did not become generalized, and secondly, an even more interesting group, those patients in whom, although Cl. *Welchii* was grown from the blood, there were no symptoms of a severe infection due to this organism.

GROWTH CHARACTERISTICS

Both surface colony form and the type of growth produced in a mixture of equal parts of normal horse serum and 1 per cent neopeptone-water were recorded. Colony

form was studied on plates made from Huntton's hormone agar and defibrinated rabbit's blood. The plates were incubated for 48 hours in anaerobic jars containing calcium chloride. The growth in serum-neopeptone-water was recorded after 20 hours incubation in the anaerobic jar. The colony form on the surface plates was recorded as smooth, intermediate smooth, intermediate rough or rough (in descending order of smoothness) and the growth in serum-neopeptone-water as non-granular or granular (see Butler¹).

Two hundred and ninety strains of Cl. *Welchii* isolated from abortifol cases were studied in this way. This number included the 110 strains reported in 1941. In those cases in which more than one culture of Cl. *Welchii* was obtained from the same patient differences were not observed between the various strains. For this reason the results with only one strain from each patient are recorded.

Considerable cultural variation was observed, as can be seen from Table I. Strains giving smooth or intermediate smooth surface colonies usually produced a non-granular type of growth in serum-neopeptone-water, while rough or intermediate rough variants gave a granular growth. Thirteen of the strains were unstable in regard to colony form, each strain producing more than one type of colony on the surface plates. These strains were classified according to the predominant type of colony.

A significant relation was observed between the cultural characteristics of the infecting strain and the nature of the patient's illness.

Reference to Table II shows that all but 2 of the 30 strains obtained from the severe cases with jaundice gave smooth surface colonies and a non-granular type of growth in serum-neopeptone-water, whereas not one of the 5 strains from the severe infec-

TABLE I THE GROWTH CHARACTERISTICS OF 290 STRAINS OF *Cl. Welchii*

Growth characteristics		
Surface colony form	Growth in serum-neopeptone-water	No. of strains
Smooth	Non-granular	77
Smooth	Granular	9 (4 unstable)
Intermediate smooth	Non granular	45 (2 unstable)
Intermediate smooth	Granular	21 (5 unstable)
Intermediate rough	Non granular	7 (2 unstable)
Intermediate rough	Granular	114
Rough	Granular	17
		290 Total

TABLE II RELATION BETWEEN GROWTH CHARACTERISTICS AND TYPE OF INFECTION

Growth characteristics		35 patients with severe generalized <i>Cl. Welchii</i> infection		40 patients with <i>Cl. Welchii</i> infection localized to the uterine contents	15 patients with <i>Cl. Welchii</i> in the blood but without symptoms of severe infection
Surface colony form	Growth in serum-neopeptone-water	30 with jaundice	5 with collapse		
Smooth	Non-granular	28	0	10	3
Smooth	Granular	1	1 (unstable)	0	0
Intermediate smooth	Non-granular	1	0	7	4
Intermediate smooth	Granular	0	4 (unstable)	4	0
Intermediate rough	Granular	0	0	19	8

tions characterized by collapse was of this type. The latter 5 strains were all unstable in regard to colony form and all produced a granular growth in serum-neopeptone-water.

Of the 40 strains from patients in whom the *Cl. Welchii* infection did not spread beyond the contents of the uterus, only 10 showed the same cultural characteristics as those strains usually recovered from the severe cases with jaundice, and not one resembled the unstable variants recovered from the patients with collapse. With the strains from the 15 patients with positive blood cultures but without the symptoms

of a severe infection, the results were of a similar order, the strains from 3 resembling those commonly causing the severe infections with jaundice.

The other 200 strains similarly studied were isolated from the vagina in patients in whom either *Cl. Welchii* was not present in the uterine contents, or in which the data were insufficient to determine whether or not this organism was present in the contents of the uterus. Of these 200, only 36 gave perfectly smooth surface colonies and a non-granular type of growth in serum-neopeptone-water, thus resembling the great majority of the strains causing

the severe infections with jaundice, and only 8 were unstable in regard to colony form and therefore could be confused with those from the patients with collapse without jaundice

CAPSULATION IN BROTH CULTURES

When the Cl *Welchii* strains were grown in Wright's broth containing minced veal varying amounts of capsular material were produced. As previously reported,¹ the staining of smears from such cultures by Richard Muir's method enabled the strains to be divided into three groups, namely, those heavily capsulated, those moderately capsulated and those showing little or no capsular material

rough strains produced more than a small amount of capsular material

There was good correlation between the degree of capsulation and severity of infection

Reference to Table III shows that every one of 33 strains causing a severe generalized infection was heavily capsulated. Whereas, of the 33 strains associated with infections localized to the uterine contents only 5 were heavily capsulated. Of the 12 strains recovered from the blood of patients who did not show the symptoms of a severe infection due to Cl *Welchii*, only 1 was heavily capsulated, 8 showed a moderate amount of capsular material and the remaining 3 practically none

Among the other 562 strains of Cl *Wel-*

TABLE III RELATION BETWEEN CAPSULATION AND TYPE OF INFECTION

		Capsulation		
		Heavy	Moderate	Slight or absent
33 patients with severe generalized Cl <i>Welchii</i> infection	29 with jaundice	29	0	0
	4 with collapse	4	0	0
33 patients with Cl <i>Welchii</i> infection localized to the uterine contents		5	14	14
12 patients with Cl <i>Welchii</i> in the blood but without symptoms of severe infection		1	8	3

Of 640 strains (including the 240 previously reported) which were examined in this way, less than 10 per cent were heavily capsulated, 25 per cent were moderately capsulated and the remainder produced little if any capsular material

Two hundred and fifty of these 640 strains were studied culturally. Practically all the strains which gave smooth or intermediate smooth surface colonies and non-granular growth in serum-neopeptone-water were heavily or moderately capsulated, while only a few of the intermediate rough or

chii examined for capsules, there were only 22 which were heavily capsulated, and 11 of these strains were from patients in whom, although Cl *Welchii* was present in the vagina, it did not gain access to the uterine contents

The correlation observed between capsulation and severity of infection was sufficiently close to justify a classification of the strains isolated from abortifacient cases into "probably highly pathogenic," (heavily capsulated), "potentially pathogenic" (moderately capsulated), and "probably

not pathogenic" (only slightly capsulated), the term pathogenic being used in the sense of being able to give rise to a severe clinically recognizable infection

PRODUCTION OF α TOXIN

The work of Seiffert,³ Nagler⁴ and Macfarlane and others⁵ on the effect of Cl Welchii toxin on human serum and lecitho-vitellin has given us a simple means of measuring the amount of α toxin produced *in vitro* by different Cl Welchii strains

The filtrates from 95 recently isolated strains of Cl Welchii were tested in this manner. The strains were grown for 18 hours at 37°C in Wright's broth containing minced veal. The cultures were centrifuged for 10 minutes at 3,000 revs per minute and the supernatant fluid filtered through a Seitz filter. The size of the inoculum, the amount of culture medium, the amount filtered and the size of the filter pad were kept constant. When human sera were used in the test they were obtained from three healthy

pared by Macfarlane *et al*). The mixtures with serum were incubated for 20 hours at 37°C and those with lecitho-vitellin for 2 hours. The test with lecitho-vitellin was four to five times more sensitive than that with human serum. When both methods were used there was good agreement for which reason only the results with human serum are reported here.

Reference to Table IV shows that wide variation occurred in the amounts of α toxin produced under these conditions.

If the strains are divided into two groups according as the maximal dilution of filtrate reacting with human serum was 1 to 12 or higher, or less than 1 to 12, and if toxin production is compared with growth characteristics as in Table V, a relation is apparent between the amount of α toxin produced and the growth characteristics of the strains.

Large amounts of α toxin were produced by 27 out of the 36 strains giving smooth surface colonies and non-granular growth in serum-neopeptone-water, and by 11 out of

TABLE IV THE RELATIVE AMOUNTS OF α TOXIN PRODUCED BY 95 STRAINS OF CL WELCHII

	No reaction with human serum	Maximal dilution of filtrate reacting with human serum									
		1/1	1/2	1/3	1/4	1/6	1/8	1/12	1/16	1/24	1/32
No. of strains	3	4	6	5	5	15	16	11	19	10	1

young women, members of the laboratory staff, whose sera had an approximately equal sensitivity to Cl Welchii toxin, since it had been noted that the sera from different individuals varied appreciably. No attempt was made to determine the maximal amount of toxin produced by varying the media or the time of incubation, since we were here concerned only with the relative amounts produced by the different strains.

The filtrates were tested undiluted and in varying dilutions, with an equal quantity of human serum or lecitho-vitellin (as pre-

pared by Macfarlane *et al*). The 26 strains giving intermediate smooth colonies and non-granular growth in serum-neopeptone-water. Among the 33 strains which showed more rough characteristics, there was only one which produced a large amount of toxin.

Although the best producers of α toxin were predominantly smooth strains, some strains were encountered which, although giving typically smooth surface colonies and non-granular growth in serum-neopeptone-water, produced very little α toxin. With one of the smooth strains studied it

TABLE V RELATION BETWEEN α TOXIN PRODUCTION AND GROWTH CHARACTERISTICS

Growth characteristics		Maximal dilution of filtrate reacting with human serum	
Surface colony form	Growth in serum-neopeptone-water	1 to 12 or higher	Less than 1 to 12
Smooth	Non-granular	27	9
Intermediate smooth	Non-granular	11	15
Intermediate smooth	Granular	1	7
Intermediate rough or rough	Granular	0	25

was impossible to detect any toxin at all with the technique outlined above, and there were four other smooth strains filtrates of which failed to react at dilutions greater than 1 to 2

The relation between capsulation and the production of α toxin is not clear. Although all of the strains which produced large amounts of α toxin were at least moderately capsulated, there was a group of very heavily capsulated strains which produced very little of this toxin. If the capsular

definite correlation was observed between the amount of α toxin produced *in vitro* by the infecting strain and the occurrence of blood destruction in the patient. Reference to Table VI shows that the filtrates from all of the 19 strains obtained from patients with jaundice reacted with human serum at a dilution of at least 1 to 12. On the other hand, with the filtrates from 3 strains which had caused severe infections associated with collapse without blood destruction, the highest dilution of filtrate at which positive

TABLE VI RELATION BETWEEN α TOXIN PRODUCTION AND TYPE OF INFECTION

		Maximal dilution of filtrate reacting with human serum	
		1 to 12 or higher	Less than 1 to 12
22 patients with severe generalized Cl. Welchii infection	19 with jaundice	19	0
	3 with collapse	0	3
15 patients with Cl. Welchii infection localized to the uterine contents		7	8
13 patients with Cl. Welchii in the blood but without symptoms of severe infection		4	9

material of all Cl. Welchii strains is of similar composition we must conclude that the amount of capsular material produced by a particular strain is not correlated with the amount of α toxin produced *in vitro*.

Among the cases of severe infection a

reactions with human serum were obtained was 1 to 6, 1 to 3 and 1 to 2 respectively.

With the strains from the two control groups there was no uniformity in regard to the amount of α toxin produced, nor could the strains in these groups be sharply

differentiated from those causing the severe infections on the basis of the α toxin produced. Among the 15 strains causing the localized infections there was one which failed to produce any detectable α toxin, while the filtrate from another strain produced opalescence with human serum in a dilution as great as 1 to 24. Similarly, with the control strains from the blood, there were two which produced so little α toxin that the filtrates failed to produce opalescence if diluted more than 1 to 2, while another strain from the blood gave a positive reaction at 1 to 24.

While in the severe generalized infections the amount of α toxin produced by the infecting strain determines whether the patient will show symptoms of blood destruction, high toxicity alone does not render a strain capable of causing a severe infection.

PHAGOCYTOSIS BY HUMAN LEUCOCYTES

One of the more recent lines of investigation was the study of the behaviour of human leucocytes towards freshly isolated strains of *C. l. Welchii*.

The white cells in freshly drawn defibrinated human blood were concentrated by the removal of portion of the plasma and red cells. An 18-hour culture of the strain to be tested was then added to this modified blood and the mixture incubated at 37°C with frequent shakings (or placed on a slow moving wheel). Smears were made after varying periods of incubation and were stained with Leishman's stain.

Sixty-five strains were tested in this fashion and considerable variation was observed, some strains being almost completely resistant to phagocytosis while others were taken up by the neutrophil polymorphs almost at once.

With this small number of strains significant relation was not apparent between growth characteristics and phagocytosis,

but a correlation was observed between capsulation and resistance to phagocytosis. Table VII shows that 22 out of 28 heavily capsulated strains were resistant to phagocytosis, whereas only 5 out of 16 moderately capsulated strains and 2 out of 21 poorly capsulated strains were similarly resistant.

TABLE VII RELATION BETWEEN PHAGOCYTOSIS AND CAPSULATION

	Phagocytosis		
	Absent or very slight	Slight	Marked
Heavily capsulated	18	4	6
Moderately capsulated	2	3	11
Slightly capsulated	0	2	19

It was also noted that after some months of artificial cultivation the resistance to phagocytosis of some strains was much diminished, although there was no detectable diminution in the amount of capsular material produced in broth.

Resistance to phagocytosis was not dependent on the amount of α toxin produced. Among the strains tested there were 4 which produced but little α toxin and yet were completely resistant to phagocytosis, while 10 strains which produced large amounts of α toxin were readily taken up by the leucocytes. These findings are in keeping with the observation that the addition of *C. l. Welchii* antitoxin to the mixture of blood and resistant *C. l. Welchii* usually resulted in but little increase in the number of bacilli phagocytosed.

On the other hand, the effect of the appropriate anti-bacterial serum on phagocytosis was very striking. In experiments in which 100 leucocytes ingested less than 10 bacteria after 1 hour's incubation, the addition of the corresponding anti-bacterial serum resulted in the phagocytosis of 500 or more bacteria by the same number of leucocytes.

Since some antigenic similarity was demonstrated among the strains causing the severe generalized infections, this section of the investigation is being continued in order to determine the possibility of using an anti-bacterial serum in the treatment of these patients

Among the freshly isolated strains tested with human leucocytes there were 16 from patients suffering severe generalized infection, 15 from localized infections and 12 isolated from the blood of patients without symptoms of severe infection. The results obtained with these strains are given in Table VIII

Only one of the strains from the severe

primarily generalized infections, it was thought that the strains from such cases must be highly invasive, and that, therefore, unlike the strains of Cl Welchii described in the text-books and the bacteriological publications dating from the first World War, they would be capable of initiating infection in experimental animals when washed free from toxin or grown on agar slopes. This proved to be the case.

Strains were grown on agar for 18 hours and the resulting growth was washed once and resuspended in saline at an opacity corresponding to 2,000 millions per c c. Varying quantities of this suspension were injected intramuscularly into guinea pigs

TABLE VIII RELATION BETWEEN RESISTANCE TO PHAGOCYTOSIS AND TYPE OF INFECTION

		Phagocytosis		
		Absent or very slight	Slight	Marked
16 patients with severe generalized Cl Welchii infection	13 with jaundice	9	3	1
	3 with collapse	3	0	0
15 patients with Cl Welchii infection localized to the uterine contents		3	3	9
12 patients with Cl Welchii in the blood but without symptoms of severe infection		2	3	7

cases was well phagocytosed, whereas 16 of the 27 strains from the control groups were extremely susceptible to the action of the leucocytes. These results show that resistance to phagocytosis is characteristic of the strains causing the severe infections but that this property does not belong exclusively to such strains.

PATHOGENICITY OF WASHED CULTURES FOR GUINEA PIGS

Since the severe Cl Welchii infections associated with abortion appeared to be

Every one of 14 strains from cases of severe infection proved capable of causing a fatal infection when 0.5 c c. of the saline suspension was injected into guinea pigs weighing 300 gms. and all but 3 strains produced death when the dose was 0.2 c c. But an appreciable number of the strains which did not cause severe generalized infections were similarly pathogenic for guinea pigs when washed cultures were used. Thus of 10 strains isolated from the blood of patients without symptoms of severe infection, 6 produced a fatal infection in guinea pigs.

when washed bacilli were injected, and of 8 strains causing infections localized to the uterine contents, 6 were similarly pathogenic

All but one of the 26 strains capable of causing a fatal infection in guinea pigs when washed bacilli were injected intramuscularly were heavily or moderately capsulated, but some of the strains which were not pathogenic for guinea pigs under these conditions were also well capsulated. It was also observed that after 6 to 12 months of artificial cultivation some strains tended to lose the power of initiating infection when washed cultures were used, which fact possibly explains the discrepancy between the findings here recorded and the apparently universal teaching that washed *Cl. Welchii* are not pathogenic for guinea pigs

Since these observations on the pathogenicity of washed cultures for guinea pigs are of great interest in connexion with the development of *Cl. Welchii* infection in general, this work is being extended and will be dealt with more fully in a later publication

CERVICAL SMEARS

The observations so far considered were made with *Cl. Welchii* grown in artificial media. For this reason I attach special importance to the observations which were made of smears from the cervical canal, since these smears afforded an opportunity of studying the morphology of the infecting strain in the tissues of the patient and also of observing the possible interaction between the patient's leucocytes and the infecting strain

In the well-established severe *Cl. Welchii* infections the cervical smears showed considerable numbers of heavily capsulated bacilli and, in addition, revealed damage to the leucocytes. There was little or no phagocytosis (Butler²)

Cervical smears from 28 cases of severe generalized *Cl. Welchii* infection have now been examined, and every one of the smears has shown these features. Among 52 control patients consisting in either those having localized infections, or those with *Cl. Welchii* in the blood stream but without the symptoms of a severe infection, this combination of many heavily capsulated bacilli and damage to the leucocytes has never been observed

In smears from some of the control patients many capsulated *Cl. Welchii* were present but they were not accompanied by appreciable damage to the cells

In those patients in whom the cervical smears showed only a few heavily capsulated *Cl. Welchii*, either with or without some damage to the leucocytes, interpretation was difficult unless a second smear was obtained. Up to the present I have encountered 12 such cervical smears. Ten of these smears were from patients who did not develop a severe *Cl. Welchii* infection and in 6 cases a second cervical smear was obtained within 24 hours of the first. Only one of the second smears showed a considerable increase in the number of *Cl. Welchii* and not one showed evidence of increased cell destruction. In both the remaining 2 cases, the first smear examined showed a few *Cl. Welchii*, some very heavily capsulated, and some damage to the leucocytes, but in each of these cases a second smear taken 12 hours after the first showed a great increase in the number of *Cl. Welchii* and also increased damage to the cells. Both these patients developed a generalized infection and died

The presence in the cervical smear of a few heavily capsulated *Cl. Welchii*, especially if accompanied by some damage to the leucocytes, suggests the possibility that a severe *Cl. Welchii* infection may develop and indicates the need for a second smear within 12 hours of the first, or earlier if the

patient develops any of the symptoms regarded as characteristic of a severe infection due to Cl Welchii

As already pointed out in a previous publication (Butler²), differences were observed in the smears from patients with jaundice and those from patients characterized by collapse without jaundice. In smears from the former, the Cl Welchii tended to be short and stout and the capsular material was fragile without a clearly defined outline, whereas in the patients with collapse the Cl Welchii seen in the cervical smear were longer and often thinner, and the stained capsular material was not so fragile and had a clearly defined outline

DISCUSSION

A study of a large number of strains of Cl Welchii isolated from abortifacient cases showed that the severe generalized infections were caused by two distinct and recognizable variants and that the nature of the patient's symptoms was correlated with the characteristics of the infecting strain

The strains causing the severe infections characterized by jaundice produced smooth surface colonies, non-granular growth in serum-neopeptone-water, heavy capsules in meat broth and large amounts of α toxin *in vitro*, they were resistant to phagocytosis by human leucocytes and were pathogenic for guinea pigs when washed cultures were used. In the cervical smears from patients infected with such strains the bacilli were surrounded by fragile capsules and there was evidence of considerable damage to the leucocytes

The strains causing the severe infections in which collapse was the outstanding symptom differed from those isolated from cases with jaundice in three ways. Firstly, surface colonies were unstable and typically smooth colonies did not predominate, secondly, these strains produced only small amounts of α toxin and thirdly, the capsules

observed in the cervical smears were not fragile but clearly defined

Only a few strains having all the characteristics of either of these two variants were encountered, apart from the cases of severe infection, and when such strains were met with they were usually present only in the vagina

When the various characteristics of the Cl Welchii strains were considered singly there were always some strains from the control cases which resembled those from the severe infections, but the more characteristic studied the less this overlap became. Thus of 11 strains obtained from the blood of patients who were not severely ill, there was not one with all the characteristics of either of the two variants so far recognized as causing the severe infections. Although 2 of the strains from this group of control cases resembled in their growth characteristics those from the severe cases of patients suffering from jaundice, only one of them was as heavily capsulated and produced as much α toxin, and this particular strain was not resistant to phagocytosis by human leucocytes. Similarly, among the strains from localized infections there was not one which resembled in all its properties either of the variants causing the severe generalized infections

As yet no work has been carried out on the amounts of "diffusion factor" (hyaluronidase) produced by the strains from abortifacient cases. While it is impossible to forecast the importance of this factor in conditioning the various types of infection associated with abortion, the extensive studies of McClean⁶ suggest that the chief rôle of "diffusion factor" in Cl Welchii infections is to facilitate local spread

It is possible that further studies of Cl Welchii strains may show that some property not considered in this paper is a more reliable index of virulence than those here recorded. But the characteristics so

far studied have established the fact that strains which differ from those causing the severe infections, produce symptoms of only a mild infection and in some cases no symptoms

Since all but one of the strains causing the severe generalized infections were heavily capsulated, resistant to phagocytosis and produced a fatal infection in guinea pigs when washed cultures were used, it appears probable that the invasiveness of the infecting strain is of paramount importance in the development of a severe abortional infection

Cl *Welchii* exotoxin *per se* is probably not of primary importance in causing a severe generalized infection. Resistance to phagocytosis was only slightly modified by the presence of Cl *Welchii* antitoxin, and strains which were highly toxigenic but unable to resist the action of the leucocytes did not cause symptoms of severe infection although actively multiplying in the uterine contents

However, the evidence in regard to the production of α toxin reported in this paper suggests that in the severe infections the nature of the patient's symptoms is mainly dependent on the type of exotoxin produced. For example, if the infecting strain produced but little of the haemolytic α toxin one would not expect gross blood destruction in the patient

If the development of a severe generalized Cl *Welchii* infection depends primarily on the invasiveness of the infecting strain and if the production of toxin alone does not enable a strain to cause such an infection, then local conditions in the genital tract are not likely to be of primary importance in the initiation of a severe Cl *Welchii* infection. Wringley⁸ writing on puerperal Cl *Welchii* infections maintained that for severe maternal infection to occur not only were intrauterine manipulations necessary to introduce the infection into the uterus,

but also that the maternal tissues must be damaged and the child dead at the time of the manipulations

This contention that a large amount of dead tissue is necessary for the development of a severe Cl *Welchii* infection was supported by Lash⁹ but criticized by Toombs¹⁰ and Hill¹¹ on the basis of their reports of fatal puerperal infections in which the mother was delivered of a living child

In the abortional cases observed in this hospital, there was no evidence of a greater amount of dead tissue in the uterus or of more extensive damage to maternal tissues in those patients who developed a severe Cl *Welchii* infection, than in those in whom Cl *Welchii* multiplied in the uterine contents without causing a severe infection

While agreeing with the suggestion that the development of a severe Cl *Welchii* infection may depend on the presence of some devitalized tissue, it should be stressed that the majority of such infections occur in the absence of such a large amount of dead tissue as that occasioned by the death of the foetus. Also, it has been the experience in this hospital that no matter what the local conditions in the uterus, a severe generalized infection with the symptoms recognized as typical of these cases does not occur when the strain multiplying in the uterine contents lacks the characteristics we now recognize as typical of the highly invasive variants

Probably the most necessary factor for the development of the severe infections is sufficient interference to introduce the Cl *Welchii* into the uterus. Without mechanical interference of some kind Cl *Welchii* infections are rare. Strains resembling exactly those causing fulminating infections have been present in the vagina but not in the uterus and infection has not resulted, which is in keeping with the supposition that Cl *Welchii* does not usually gain access to the uterine contents except through interference

In the abortional cases there is no evidence that the development of a severe Cl Welchii infection is dependent on factors such as fatigue, pregnancy toxæmia or hæmorrhage, nor have we been able to show that symbiosis with other organisms either aerobic or anaerobic is important in the causation of the severe infections.

The comparative rarity of the severe generalized Cl Welchii infections is readily explained by the finding that the highly virulent variants are only a very small minority of the Cl Welchii strains recovered in abortional cases. In this hospital during the last 3 years less than 5 per cent of the Cl Welchii cultivated from the vagina have been of the type responsible for the fulminating infections.

From what has been written it is clear that a complete bacteriological study of the infecting strain should be a necessary preliminary to the assessment of any form of treatment for the severe Cl Welchii infections associated with abortion. That this is seldom done is evident from reports of recent cases.

Following Bohlman's¹² report in 1937 of 3 cases of gas gangrene treated with sulphanilimide, Sadusk and Manahan¹³ treated 2 abortional Cl Welchii infections with this drug. In their opinion this treatment sterilized the blood stream and led to the patient's recovery, but there was no report of any bacteriological investigations to determine whether the infecting strains were of the type likely to cause fatal infections. And judging by the clinical descriptions of the patients it is probable that they were not the severe type of Cl Welchii infection, but merely examples of cases in which this organism was present in the blood without causing the symptoms characteristic of a severe infection. In the experience of this hospital such patients recover without treatment directed specifically to Cl Welchii (Hill and Butler¹⁴)

Baker¹⁵ reported the recovery after treatment with sulphanilimide of a patient suffering from puerperal peritonitis in which Cl Welchii was recovered from the blood and peritoneal pus. But anaerobic streptococci were also present in the peritoneal cavity, and it is possible that the latter organism was of equal or more importance in causing the patient's symptoms, which it should be pointed out did not resemble those usually reported as characteristic of the severe Cl Welchii infections. Here again there was no attempt to assess the virulence of the infecting strain bacteriologically.

The same lack of complete bacteriological investigation in regard to probable virulence is also apparent in much of the recent work carried out on the treatment of experimental Cl Welchii infections with the sulphonamides. Not one of four recent articles on this subject, namely those of Stephenson and Ross,¹⁶ Henderson and Gorer,¹ Reed and Orr¹⁸ and Otero and Gonzalez,¹⁹ contains any description of the colony form, capsulation or resistance to phagocytosis by human leucocytes of the strains employed in the experiments. Further, only one strain, the first one used by Stephenson and Ross, was described as recently isolated. It is, therefore, highly probable that with this exception, the strains used for these experiments had been considerably modified by artificial cultivation, since in my experience the properties of resistance to phagocytosis and pathogenicity of washed cultures for guinea pigs may be lost in as short a time as 6 months.

For experimental work to be truly suggestive of the probable usefulness of the sulphonamides in the severe abortional infections, it would be essential that the strains used to infect animals should have retained all the characteristics of freshly isolated strains from severe infections. Especially should caution be exercised in applying the

results of experimental infections when calcium salts or soil have been used to initiate the disease, since there is no evidence in the abortional cases that the presence of these substances is necessary for the development of a severe *Cl. Welchii* infection.

The need for strong experimental support for the therapeutic use of the sulphonamides in the severe abortional infections is readily apparent when it is remembered that some of these drugs may cause considerable renal damage (Laird,²⁰ Peterson and Finland²¹). Such complications are especially likely to occur when the urinary output is decreased, a happening almost universally present in the severe *Cl. Welchii* infections following abortion.

The close correlation observed in abortional cases between the severity of the infection and the characteristics of the infecting strain raises the question as to whether a similar correlation exists in *Cl. Welchii* infections of war wounds. In gas gangrene following wounding the mode of infection probably differs from that operating in the abortional cases. In the latter, infection must usually result from the introduction of vegetative forms of *Cl. Welchii* direct from the faeces, while in gas gangrene associated with wounds it is the general opinion that the organism is introduced into the wound in the form of spores together with fragments of soil and other foreign matter, these latter substances enabling the spores to develop in the devitalized tissue present in the wound.

Having regard to this difference in the mode of infection, I would suggest the following possibilities in connexion with gas gangrene associated with war wounds —

1. In cases in which *Cl. Welchii* is present in the wound but does not cause symptoms of infection the strain will not be a smooth variant, will be only poorly capsulated and will be very susceptible to the action of the leucocytes.

2. Many cases of severe gas gangrene will be caused by strains of *Cl. Welchii* which are not sufficiently virulent to cause the fulminating type of infection seen in connexion with abortion. In gas gangrene following wounding, interference to the blood supply, extensive tissue damage and the presence of foreign material such as soil enable these strains to set up an extensive localized infection, which, however, seldom becomes generalized in the initial stage of the disease since the infecting organism is not highly invasive in character.

3. Strains similar in virulence to those causing the fulminating abortional infections (though not of necessity the same two variants so far recognized) will be responsible for those cases of gas gangrene which follow wounds unaccompanied by interference to the blood supply and extensive tissue damage. This latter contention is supported by the fulminating character of such infections. (See Fraser²²).

While it seems likely that in gas gangrene following war wounds the part played by *Cl. Welchii* exotoxin is of more importance than in the severe abortional infections due to this organism, the recent findings of Robertson and Keppie²³ show that the toxicity of the infecting strain is not enough to account for the severity of wound infections. These authors tested the *in-vitro* toxin production of 26 recently isolated strains. The strains were from cases which ranged from acute gas gangrene to those in which *Cl. Welchii* was present in the wound without causing any recognizable symptoms. All but one of the strains from patients without symptoms of gas gangrene were of a basic toxicity equal to or above that of the strains from cases of typical gas gangrene. The authors explained these findings on the ground that in the cases without symptoms of *Cl. Welchii* infection the conditions in the wound were unfavourable for the development of this organism,

but they did not give details to substantiate this contention. I believe that a study of properties other than toxicity would have offered a more convincing explanation.

Our understanding of Cl. Welchii infections has been retarded because of too much stress on the toxæmic side of these infections. The findings that a certain proportion of Cl. Welchii strains are capable of initiating a fatal infection in the guinea pig when the inoculum consists of organisms washed free of toxin, that some strains are resistant to phagocytosis by human leucocytes and that this resistance is practically unaffected by the presence of anti-toxin but is completely removed by the addition of anti-bacterial serum appropriate to the strain concerned, show that some strains are highly invasive in addition to producing a potent exotoxin.

SUMMARY

1. All the strains of Cl. Welchii causing the severe generalized infections possessed the properties of highly invasive variants and differed from both the strains causing localized infections and those cultivated from the blood of patients without symptoms of a severe Cl. Welchii infection.

2. In the severe infections the patient's characteristic symptoms were correlated with the properties of the infecting strain.

3. The comparative rarity of the severe infections was readily explained by the finding that the highly invasive variants of Cl. Welchii formed only a small minority of the strains cultivated from the genital tract.

4. All the strains causing the severe infections and also some of the control strains produced a fatal infection in guinea pigs when washed cultures from agar were injected intramuscularly. This property was sometimes lost comparatively rapidly under artificial cultivation.

5. It is suggested that in gas gangrene following wounding a somewhat similar correlation to that observed in abortional cases may exist between severity of infection and the characteristics of the infecting strain.

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Anæsthesia and Analgesia in Obstetrics from the viewpoint of the General Practitioner

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IN the *British Journal of Obstetrics and Gynaecology*, June 1941, Griffiths and Goodall consider Obstetric Anaesthesia and Analgesia from the point of view of the specialist. But obstetrics and gynaecology form such a large part of the general practitioner's work, that his point of view must be considered too.

Obstetric anaesthesia is a most difficult subject, as we have to consider what is safe and practical for that great number of women, over half a million a year, attended sometimes in unsuitable surroundings, by general practitioners and midwives.

We are so apt to lose our sense of proportion, a series of 1,000 cases may be impressive, but it is as nothing compared with the yearly total of confinements. Let us then keep this standard before our eyes. "Is the technique we employ and the agent we use really safe for confinements all over the country?"

The recent work of Montgomery¹ in analysing the maternal death-rate in Philadelphia gave a very important part to errors of judgment in selection and technique in giving anaesthesia and analgesia in labour.

Anaesthesia is needed in obstetric practice (1) in the antenatal period, (2) during delivery, (3) after delivery.

ANTENATAL PERIOD

In the antenatal period the administration of an anaesthetic is frequently neces-

sary for an examination, for an external version, or for the induction of labour.

For an examination or for version complete relaxation is required, whereas for the induction of labour relaxation is not of primary importance, but for whatever purpose the anaesthetic is given in the antenatal period it should always be remembered that the patient has labour in front of her and that she should be frightened as little as possible.

A very large number of these antenatal procedures may take place under conditions which are far from ideal, so we must consider what is practical in the circumstances existing at the time.

AFTER DELIVERY

Anaesthesia after delivery may be required for the repair of the perineum or the removal of the placenta, and the same type of anaesthetic is required as for obstetric operations generally.

ANAESTHESIA DURING LABOUR AND FOR OBSTETRIC OPERATIONS

One should differentiate clearly between anaesthesia and analgesia. By anaesthesia I mean the complete loss of sensation. By analgesia I mean the relief of pain, but not necessarily the absence of all pain.

Now anaesthesia may be required just at the delivery in normal labour, for some operation, the most common being delivery

by the forceps, for Caesarean section, or extraction of a difficult breech presentation

When we consider anaesthesia for operative midwifery it will be convenient to take the operation of Caesarean section as a typical example, because the same considerations which apply to this operation must apply to anaesthesia in operative midwifery as a whole. The chief and most essential point is that the anaesthesia shall be as light as possible.

Opinions differ as to the anaesthetic of choice and there are several methods available (1) spinal analgesia, (2) open ether and vinesthene-ether mixture, (3) nitrous oxide-oxygen ether or nitrous oxide-trichlorethylene, (4) local infiltration, (5) chloroform.

Opinions differ greatly as to the suitability of spinal anaesthesia. In this country consensus of opinion seems against its use and there is no doubt that deaths have occurred under spinal anaesthesia, during and after Caesarean section. On the other hand, some American anaesthetists have obtained excellent results.

Batten,² from The Methodist Hospital New York, reports excellent results from spinal anaesthesia in Caesarean section. Procain was the drug most commonly used, but he reports that 16 per cent of all patients required supplementary gas and oxygen or cyclopropane. He does not advise spinal anaesthesia in cases of high blood-pressure. H. K. Ashworth,³ of Manchester, finds spinal anaesthesia from 12 c.c. of stovaine or 10 c.c. of light percaïn suitable for Caesarean section.

I would, however, like to stress the need for serving a long apprenticeship before using this method in midwifery. It is for the few, the very few. A number of deaths have occurred and will continue to occur because of lack of knowledge on the part of the administrator.

We must also ask ourselves whether we

are justified in using spinal anaesthesia for relatively straightforward operations for which a simple inhalation anaesthetic will suffice. It is perhaps a little unfortunate that we do not discuss our mistakes and misfortunes more freely. Sometimes it is only by accident that we hear of unfortunate results.

A question was recently asked in Parliament⁴ concerning the death of a young soldier from paralysis and toxemia, 7 months after the administration of a spinal anaesthetic, for repair of a hernia. Mr McLeod⁵ tells us how very nearly a patient came to dying under spinal anaesthesia, given for a simple operation. Jarman,⁶ in an analysis of 1,300 "deaths on the table" found that 81 occurred under spinal anaesthesia, as against 29 under chloroform. Van der Post⁷ tells us of "three disturbing cases under spinal anaesthesia," so that, before we submit our patients to an operation under spinal anaesthesia, we must satisfy ourselves that circumstances really demand this type of anaesthetic.

OPEN ETHER OR VINESTHENE-ETHER MIXTURE

Either ether or vinesthene-ether mixture is really excellent dropped on to an open mask. Vinesthene-ether is less irritating and is pleasant to take. The Americans speak of this method as "drip ether," not "open ether" and I think it is important to remember the difference in terms. Light ether or vinesthene-ether anaesthesia is difficult to administer by the open method, the patient either gets a little too deep or a little too light, when she may cough and start vomiting.

I think the essential to success is to drop the ether mixture on to the mask, not to pour it on. When the patient seems to be too lightly anaesthetized, a very common mistake is for the anaesthetist to pour on

more ether, whereupon the patient either coughs, goes into spasms, or vomits. All that is necessary is to increase steadily the speed of the drip.

GAS-OXYGEN-ETHER AND GAS-OXYGEN-TRICHLORETHYLENE

Gas-oxygen-ether sequence from Boyle's machine has stood the test of time. It is simple to administer and as a rule very little ether need be used.

Except for the lower segment Caesarean section, very little relaxation is required, and it is important to keep the anaesthetic light. The baby should cry the moment it is born, if it does not, the anaesthetic has been too deep, or there has been some obstetric injury to the child. After delivery the ether can be turned off, the anaesthetic continued with gas and oxygen only, allowing the uterus to contract.

Recently we have a new anaesthetic, Trichlorethylene or "Trilene," and the sequence gas-oxygen-trichlorethylene is satisfactory. The induction is carried out with gas and oxygen only, and then these gases are blown over trichlorethylene which is placed in a chloroform bottle of a Boyle's machine. It is of benefit if this bottle can be slightly larger than is usually used. Gas-oxygen-trilene sequence will always suffice for delivery by the forceps.

For Caesarean section, just before the surgeon is ready to start and the dressing towel removed, I put my hand on the abdomen and ascertain how much relaxation there is. If this is insufficient, I turn on a little ether until I am satisfied as to the relaxation. I turn off the ether as soon as possible. I have found that the baby always cries immediately when born if this method is used.

The anaesthetic is continued with gas-oxygen-trichlorethylene until just before the peritoneum is closed. It may then

be necessary to add a little ether to prevent the intestines getting in the way, although this is not usually the case. It is most noticeable how well the uterus contracts after gas-oxygen-trichlorethylene anaesthetic. There is very little vomiting and the patient is so well next day.

CYCLOPROPANE

Some anaesthetists are enthusiastic about cyclopropane anaesthesia for obstetric operations and there can be no doubt that this is an excellent anaesthetic in proper hands, but it is a most difficult anaesthetic to use and requires experience. Cyclopropane anaesthesia is too difficult for general use.

LOCAL INJECTION

Eardley Holland⁹ advocates local infiltration analgesia for Caesarean section. He does not like premedication, but when he uses this he prefers rectal paraldehyde. He feels, however, that it is important to get the absolute co-operation of the patient and to explain what is going to be done.

For injection he uses $\frac{1}{2}$ per cent procain in saline with no adrenaline. About 100 c.c. are used for infiltration beneath the skin of the abdominal wall. The skin is incised down to rectus sheath and about 100 c.c. then used for infiltrating rectus sheath on each side of midline, taking good care to put plenty behind the symphysis pubis. A little gas and oxygen can be used if necessary for suturing the abdominal wall. The technique⁹ is not easy and is for the few, not for general use.

CHLOROFORM

I would devote just a little time to chloroform. Chloroform is so cheap, gives such an extremely satisfactory anaesthesia, is so portable, that it would appear to be the ideal

anaesthetic for obstetric use Now what are the objections (1) in normal labour chloroform slows down the pains and may bring labour to an end, (2) chloroform relaxes the uterus, leading to postpartum haemorrhage and a soft uterus that will not contract after delivery, (3) chloroform may cause death from primary cardiac failure or from an over-dose, (4) chloroform may cause death from readministration, for example, if chloroform has been given to produce analgesia, for the relief of pain, it may be used to produce full anaesthesia for doing repair of the perineum, and several deaths have been recorded from such a procedure, (5) chloroform may cause death from damage to the liver (delayed chloroform poisoning) Patients who have had a long labour are particularly susceptible to delayed chloroform poisoning They have been in labour perhaps for 3 or 4 days in some country cottage During this time they have been starved and then delivered by the forceps under chloroform anaesthesia, perhaps deep chloroform anaesthesia About the 3rd day the patient becomes jaundiced, starts to vomit and dies, and a necrosis of the liver is found Delayed chloroform poisoning is much more common than is generally imagined

Obstetric operations very often take place in the home or in some small nursing home and the difficulty of carrying apparatus about presents a real difficulty With a little forethought and ingenuity, however, the necessary apparatus can be cut down to a minimum The operation is likely to be short and one does not require to carry a number of heavy gas cylinders A simple stand carrying one full gas and one full oxygen cylinder should suffice Flow meters and Boyle's bottles can be carried separately and put together at the bedside A simple apparatus of this kind is most valuable and one cannot over-stress the value of gas and oxygen in midwifery

ANALGESIA IN NORMAL LABOUR

A more difficult problem is the relief of the pain of labour in the large number of confinements conducted by midwives in homes without the presence of a doctor The number of patients who are confined in hospital is steadily increasing, and hospital committees are reluctant to provide anaesthetists to attend normal confinements Again, most patients who are attended by general practitioners cannot afford to pay for a specialist in anaesthetics For these patients a method that is practical and safe and can be administered by the midwife is essential

The suffering of the patient in labour may be divided into two stages the 1st, when the pains are not severe and the 2nd when they are severe and frequent For primiparae this 2nd stage starts shortly before full dilatation of the cervix, and for multiparae at about dilatation of the cervix to the size of a 5/- piece If an inhalation analgesic is used too early in labour, the cost of gas becomes heavy, so reliance must be placed on some sedative drug Sedative drugs used are potassium bromide and chloral mixture, morphine, morphine and hyoscine, avertin, paraldehyde, nembutal, sodium soneryl, and, more recently, pentothal, but whatever our choice of drug certain requirements remain

DRUGS IN THE FIRST STAGE

The requirements are that (1) the drug should give prolonged analgesia with the minimum of repeated doses, (2) the patient should sleep between the pains, but should rouse during them, (3) labour should not be prolonged, (4) the child should suffer no ill-effects from absorption of the drugs used

(a) *Potassium-bromide-chloral* These are usually given with an initial dose of 30 grains of each, repeated in similar doses

at 3 and 4 hourly intervals. The analgesic action of these drugs is not of great value, but their sedative action is of value.

(b) *Morphine* This is the most valuable sedative drug for use during labour and is probably the safest. Morphine should be given early in labour by injection in a dose of $\frac{1}{4}$ grain for primiparae when the cervix is dilated to admit two fingers and for multiparae when the cervix will admit one finger.

Louise McIlroy and Helen Rodway (1933),¹¹ found that contrary to the belief of many obstetricians morphine had no ill-effect on the infant, but that spontaneous respiration occurred at birth in the majority of cases, however late morphine was administered. It is remarkable how little notice has been taken of this very important work.

(c) *Paraldehyde* given *per rectum* dissolved in olive oil with a dosage of 60 minims per 14 pounds of body-weight with a maximal dose of 1 ounce, has been recommended by some observers, but this drug, when tested by a committee of the British College of Obstetricians and Gynaecologists,¹² did not meet with approval. Rectal analgesia is not really satisfactory in labour.

(d) *Morphine and Hyoscine* Morphine $\frac{1}{4}$ gr with hyoscine 1/150 gr is given early in labour. Afterwards hyoscine 1/450 gr is given at intervals of from 2 to 4 hours, depending on the patient's reaction. The use of this technique commonly known as "twilight sleep" does require great experience. It is sometimes found that the patient becomes excited and quite beyond control.

(e) Powerful sedative drugs known as basal narcotics have been found extremely useful for premedication in general surgery, and their use in midwifery has been advocated by some workers, but it cannot be denied that they have disadvantages and possible dangers. Potassium-bromide-chloral, and morphine remain the only

really safe sedative drugs for everyday midwifery. It is most marked how the United States anaesthetic journals contain more and more warnings against over-sedation in midwifery.

Many observers have published satisfactory series of cases in which pain has been relieved by powerful sedative drugs, but until some authoritative large-scale investigation as to their safety is carried out, these should be restricted to hospital midwifery and the practice of the experienced anaesthetist.

THE SECOND STAGE OF LABOUR

We now come to the 2nd stage of labour in which an inhalation anaesthetic is suitable. Much of the present knowledge of inhalation methods of relieving pain in labour has been learned owing to the encouragement given by Lady Baldwin and Lady Rhys Williams and their friends in the National Birthday Trust Fund, who, over a number of years, have striven so energetically to find safe and practical methods of alleviating pain.

Whatever anaesthetic agent we use, or whatever machine we make use of, the following conditions are necessary:

(1) the apparatus used must be simple and not get out of order, (2) the method of administration can be used by the mother with a midwife supervising, (3) labour must not be delayed, (4) the patient must not get excited, (5) the anaesthetic agent must have no ill-effect on mother or child.

For inhalation agents we are confined to chloroform and nitrous oxide gas and lately, Trilene (Trichlorethylene). Other drugs have been used, but all have disadvantages which cannot be overcome in everyday midwifery.

CHLOROFORM

Chloroform is cheap, is easily portable, but a committee of the British College of

Obstetricians and Gynaecologists,¹² who carried out a comprehensive test of various methods to obtain relief from pain, regretfully come to the conclusion that there is no way in which chloroform can be made reasonably safe for producing obstetrical analgesia for that large number of women attended by midwives

NITROUS OXIDE

To obtain complete relief from pain in normal labour a mixture of nitrous oxide and oxygen should be administered. The technique of the administration is not difficult and should not be beyond the ability of any general practitioner or of a midwife working under supervision. Expensive apparatus is not necessary, but with a high proportion of patients the gas and air technique from an automatic apparatus devised by Minnitt will suffice. In fact Minnitt¹¹ of Liverpool, by his gas and air apparatus, has solved many of the difficulties which stood in the way of providing relief from pain for all women.

In the official test carried out by the committee of the Royal College of Obstetricians and Gynaecologists,¹² it was found that 77 per cent of patients did obtain adequate relief from the administration of gas and air analgesia. I have personally closely observed the use of gas and air at the Wellhouse Hospital, Barnet, since 1933, and I am satisfied that if it is found that a reasonable degree of relief is not being obtained from gas and air we should ask, not what is wrong with gas and air, but what is wrong with the administration?

To obtain really satisfactory relief the closest attention to minute details is absolutely necessary. The facepiece from which the patient inhales must be a really close fit and she must know how to use it. It is essential to see that there is gas in the cylinders and that the apparatus is in perfect order. If these details are attended to, the

Minnitt apparatus is a satisfactory means of relieving the pains in the 2nd stage of labour, when the midwife alone is in charge.

For the case attended by the general practitioner gas and air will generally suffice, but the practitioner who wishes, and undertakes to give, absolute relief from pain must use nitrous oxide and oxygen in about 30 per cent of cases. This 30 per cent will consist of the very nervous patient, the non-co-operative patient, and the patient who demands complete oblivion. The adoption of gas and air analgesia in labour will assist the busy general practitioner as much as his patient. In most cases he will not be obliged to spend many hours at the bedside of his patient, and by those of us who are not enthusiastic nocturnal obstetricians this relief will be appreciated.

*TRILENE AND TRICHLOROETHYLENE

I was impressed by the value of trichlorethylene for producing light anaesthesia in general surgery, and on Langton Hewer's suggestion I decided to investigate its value in midwifery.

ANALGESIA IN LABOUR

For the relief of pain in normal labour, trichlorethylene is undoubtedly very effective, but I am not sure that it fulfils all the conditions which would be required for its general adoption, outside hospital practice. I have administered this drug to a number of patients in hospital and private practice, but not sufficient to come to a definite conclusion as to its safety.

My friend, Dr Hudson, Obstetric Surgeon, North Middlesex Hospital, Edmonston, was so very kind as to try out trichlorethylene over a number of cases. The method of administration was to use an ether bottle

* Trilene is trade name of specially purified trichlorethylene

with an inlet and outlet and three-way gas stopcock, the outlet being connected by corrugated tubing to a facepiece, which was given to the patient who then was told to apply the facepiece to her face and to breathe in and out

Hudson found that trichlorethylene produced a fair amount of analgesia in many cases, this was better than an analgesia obtained from gas. He found that labour pains were sometimes slowed down and on two occasions, when continuous Trilene and air was given towards the end of labour with the idea of obtaining analgesia sufficient to perform episiotomy, at the end of the next pain, he found that the next pain did not come until another 7 or 8 minutes, whereas the previous interval between the pains had been 2 minutes. The patients did not feel anything while the episiotomy was performed. One or two of the patients went into a condition closely resembling a drunken stupor and were not co-operative. Hudson's conclusions are that Trilene produces satisfactory analgesia, but that in view of the slowing down of the pains, it is inferior to gas, which stimulates the pains.

He also feels that he has not yet been able to collect enough cases to give a final verdict. My own conclusions based on a relatively small number of cases, are the same as Hudson's. I did find that there were longer intervals between the pains in some cases and one or two patients became excitable, but a satisfactory analgesia seemed to depend on a satisfactory dosage. I found that it was very easy to give a relative overdose and to bring labour pains to an end as with chloroform, but the pains very rapidly came back again after the administration was discontinued.

I first started by putting 3 ounces of Trilene into the bottle, but I found after trial that the dose should not exceed 1 ounce to the bottle and this 1 ounce would last about an hour to an hour and a half. The analgesia

is very effective and a continuous Trilene and air during the actual birth gives complete relief. So far I have noticed no ill-effect on mother or child.

I feel that the apparatus can be improved, but that the time has not yet come when Trilene analgesia can safely be used by a patient under the supervision of a midwife. I believe that the delay of uterine contractions can be overcome by correct dosage and that this dosage can easily be found after a long series of cases which it is very difficult to collect at the present time.

There is one remarkable difference between Trilene and chloroform. If too much chloroform is administered, uterine contractions are slowed down or completely abolished for a considerable time, but when Trilene is being used, the slowing down is only for a question of 10 minutes or so, and if the Trilene is withheld for one or two pains, the contractions return with increasing vigour.

Claye, in his book on Obstetric Anaesthesia, asks a very pertinent question. Why, he says, over the country as a whole, are not the pains of labour more freely relieved? The answer is that anaesthesia and analgesia in obstetrics is not only a medical problem but a sociological one. At the fees paid to-day, midwifery for the general practitioner is not really an economic proposition, and if he is engaged in National Health Insurance Practice on a large scale, he simply has not the time to give to midwifery.

There is also the regulation, a wise one, made by the Central Midwives Board, that a second responsible person must be present when analgesia is administered by a midwife.

It is very noticeable that if one looks on the map at the "black areas" of high maternal mortality,¹⁴ one finds that these coincide with the districts where conditions of general practice are most unsatisfactory. Midwifery should be the province of a

limited number of general practitioners who are genuinely interested in the work and who are given time to do the work. Nothing can be more unsatisfactory than the present practise adopted by many Local Authorities. These bodies appoint what they call a District Maternity Officer, but she cannot rightly be described as a Maternity Officer at all. She should be called an Antenatal Examiner, because this is all that she does.

She sees those patients who have engaged only a midwife to attend them in their homes in the confinement and she carries out the antenatal work. This she does very well, but she finishes for the day at 5 p.m. and should anything go wrong during a confinement, the patient's own doctor is sent for. He does not receive any warning and he is called upon then to deal with some grave obstetrical emergency, under conditions which are far from satisfactory.

If then we are to provide a reasonable degree of relief from pain in labour for all women in this country, we must completely reorganize our maternity services, and we must take into account the general practitioner and the midwife. Whatever scheme we may adopt, the midwife will remain the one essential factor, a method of giving

relief from pain in labour is not of any real value unless it can be administered by the midwife.

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Tuberculosis of the Female Genital Tract

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TUBERCULOUS disease of the female genital tract has been the subject of many communications, and is discussed in all modern Gynaecological text books. It is still a somewhat mysterious complaint because of its silent onset, the absence of typical symptoms and the difficulty in giving any satisfactory forecast as to the likely course of the disease and its complications. Treatment of the condition is also far from being either agreed or satisfactory.

AETIOLOGY

Although uncertain, nevertheless it is believed that with few exceptions a primary focus exists usually in the lungs. Jameson¹ gives the incidence of pelvic tuberculosis as 8 per cent in cases of active pulmonary tuberculosis, which is a formidable figure.

Lackner, Schiller and Tulsky² regard the spread as *via* the blood stream, Moura³ gives several reasons in favour of the infection being ascending in character, Schoedel⁴ suggests inherited and general tuberculosis is much more common than formerly believed, Hirsch-Hoffman⁵ dogmatically claims that primary pelvic tuberculosis can occur, and consider all cases of pelvic tuberculosis as either direct spreads from peritoneum or of lymphogenic origin. From these few references it is clear that no one view is universal, despite the frequency of genital tract tuberculosis.

FREQUENCY OF SITES AFFECTED

The Fallopian tubes are most frequently

affected, and in 90 per cent of such cases the disease is bilateral.⁶ The endometrium is next and, according to King⁷ and Bush⁸ it is involved in 48 per cent of all cases of genital tract tuberculosis. Diethelm and Ramsey⁹ believe that tuberculous endometritis, with or without tuberculous myometritis, seldom exists apart from tuberculous salpingitis.

Most authors regard the ovaries as the next most frequent site, but explain that they are rarely affected by themselves, but rather as part of a chronic tubo-ovarian condition and that this is usually bilateral.

The cervix shows tuberculous lesions next in frequency. Counseller and Collins¹⁰ summarized the collected literature of the 109 such cases published up to 1935, and Stevenson¹¹ in 1938 reported 18 further cases of which he regarded only one as primary. He regards cervical tuberculosis as being present in 6 to 8 per cent of all cases of genital tract tuberculosis, and always secondary to tuberculosis of the upper genital tract. In discussing this he quotes the coincidence of tuberculous cervicitis with tuberculous salpingitis as 87 per cent, with tuberculous endometritis 24 per cent, and with tuberculous oophoritis 39 per cent.

Tuberculous vaginitis and Bartholinitis are the least frequent. McGoldrick¹² reported one case of primary tuberculosis of the vagina in 1936. Fullerton¹³, Jaworowskaja,¹⁴ Bassler¹⁵ and Hersh¹⁶ between them record 5 such cases but do not comment upon whether they were primary or secondary.

OTHER CONDITIONS PRESENT WITH GENITAL TRACT TUBERCULOSIS

It is surprising how seldom female genital tract tuberculosis exists with some other pelvic abnormality. Gais¹⁷ and Ravid and Scharfman¹⁸ between them record 29 instances of coincident uterine cancer and genital tuberculosis up to 1939. They discuss the possibility of chronic tuberculous inflammation as being an aetiological factor of the malignancy in these cases, and believe the tuberculosis had existed for some time before the carcinoma developed.

Adenomyosis with genital tuberculosis is reported by Rigdon¹⁹ but he offers no comment. Cetroni²⁰ found 8 cases in which genital tuberculosis and uterine fibroids co-existed. Stewart²¹ describes 1 case with coexistent adenomyosis, endometriosis and tuberculosis on the one site. Schiller²² has recorded 1 case of coexistent dysgerminoma and genital tuberculosis.

It is probably pertinent to remark here that were routine pathological examination of all gynaecological specimens made by competent pathologists and the findings tabulated, the coexistence of genital tuberculosis and other diseases of the genitals would be found more often.

SYMPTOMS

There does not seem to be any one combination of signs and symptoms, nor of symptoms nor of signs alone, which are at all constant. In nearly all cases the diagnosis is in doubt until the tubercles are identified naked eye at operation, or microscopically in section. It very often happens that tissue removed at operation is only identified as involved by unsuspected tuberculosis during the course of laboratory investigation. The various tests (skin reactions, guinea pig inoculations) have been given full trial, but are discouraging.

TUBERCULOUS ENDOMETRITIS

As suggested by Bush²³ routine uterine curettage affords the best hope of preoperative diagnosis. Diethelm and Ramsey²⁴ agree with this, as do Schockaert and Ferin²⁵ and the present author. The existence of tuberculous disease of the placenta as reported by Palanos²⁶ who states it is present in 5 per cent of cases in which the mother has active pulmonary tuberculosis, the reference by Schaefer²⁷ to tuberculous placentitis in the year 1939, similar remarks by Couvelaire²⁸ in 1927 and of Schoedel²⁹ in addition to the findings of McCord,³⁰ all point toward pregnancy being possible in an established case of tuberculous endometritis. The fact that tuberculous endometritis and intra-uterine pregnancy have never been found to coexist is, however, difficult to explain in view of the several cases of coexistent tubal pregnancy and tuberculous salpingitis.

TUBERCULOUS SALPINGITIS

Sterility from blockage of the Fallopian tubes is the commonest abnormality with this lesion, because of its frequency during the childbearing age. That pregnancy can occur with tuberculous disease of the tubes is evident. Stevenson and Wharton³¹ record 8 cases of tuberculous salpingitis with tubal pregnancy. Stein³² reports a 9th similar case and in his specimen there was coincident tuberculous endometritis. Busby and Fisher³³ add a 10th case without comment other than that the tuberculosis was not suspected at operation.

In 1942 Bland³⁴ reviewed all the literature to date relative to coexistent tubal pregnancy and tuberculous salpingitis, and believes 33 such cases have been confirmed. Eight occurred in multiparae, no evidence existed of any unilateral tendency of the disease, nor was one tube more frequently the site of the pregnancy than the other.

He also draws attention to the difficulty of diagnosis at operation and remarks that routine pathological examination of the specimens is the only sure means of diagnosis.

The Fallopian tubes may be patent for a long time in many cases of tuberculous salpingitis, especially when the serous coat is affected first. Patency can also exist for some time with tuberculous endosalpingitis, as has occurred within the experience of the author.

The longer standing cases of tuberculous salpingitis with gross deformity and enlargement of both tubes, with adhesions and with or without uterine misplacement, the so-called tubo-ovarian masses and cold abscesses, are more readily recognized but are of less frequent occurrence. In many such cases the differential diagnosis is from the encysted, pelvic inflammatory masses encountered in cases of old-standing peritonitis of non-tuberculous origin. In addition, the exclusion of the adherent intraligamentary or ovarian cyst, or of the chronic hydrosalpinx must also be remembered, and is difficult.

SUMMARY OF DIAGNOSIS

The one outstanding symptom of tuberculous disease of the genital tract appears to be sterility. Most cases remain free from complaint until after marriage, and it would seem that the sterility draws attention to other complaints which later lead to investigation and diagnosis of the condition. Apart from the sterility, which is usually absolute, a feeling of weight in the pelvis, some lower abdominal discomfort, vaginal discharges and menstrual irregularities with premenstrual pain appear to be most important. Complete amenorrhoea is an exception, true menorrhagia is also uncommon. The author has not found examination of vaginal discharges or bleedings

of help, even at or close to the menstrual times. In the case of tuberculous disease with an exudate in the pelvis, one case was recognized during microscopical examination of fluid aspirated through the posterior vaginal fornix.

INVESTIGATION

Any patients with symptoms suggestive of tuberculous disease should have general physical examination and routine chest X-rays to exclude any active focus. Such evidence of tuberculosis was only found in 3 of the 15 cases now reported.

Routine bimanual examination, combined with uterine biopsy or curettage, afforded the best indication of the exact nature of the cases, and in none of the cases under consideration was tuberculous endometritis found to exist by itself. Coincident tuberculous endometritis with salpingitis was proved in 7, and tuberculosis of the Fallopian tubes alone in 8 of the same 15 cases.

Although it is quite possible that tuberculous disease of the cervix was overlooked, either in the cases under review or in others not included owing to failure in diagnosis, their absence would appear to confirm the views of other writers and point toward the condition being of great rarity. Similarly, there were no cases of tuberculous vaginitis, vulvitis nor Bartholinitis.

TREATMENT

Comment is not necessary here concerning what would be done for the cases of tuberculosis of Bartholin's glands or tuberculous vaginitis, with or without cervicitis, other than to refer the reader to the works already quoted. These agree that conservative treatment yields encouraging results except in deep-seated and very chronic tuberculous disease of Bartholin's glands.

or of the cervix, which were satisfactorily treated by excision and removal

In cases of tuberculous salpingitis my practice has been to remove completely both tubes, including their interstitial portions. The ovaries have been conserved, except where extensively involved in a chronic tubo-ovarian condition

In many patients thus treated the operations have been difficult owing to widespread, dense adhesions within the pelvis itself and, in some cases, of the intestines and general peritoneal contents. In none of these, however, has there been any post-operative complication either from intestinal obstruction, post-operative ileus, nor fistula formation. The writer considers tuberculous disease of the tubes best treated by bilateral removal of the tubes with the ovary, when similarly affected. The disease has already sterilized the patient, and the writer believes that by the salpingectomy any further local or general spread is less likely

When the ovary has been but slightly involved it has been conserved, no ill-results have followed this

TUBERCULOUS ENDOMETRITIS AND/OR MYOMETRITIS

Seven cases of this type were encountered but, as hysterectomy was not performed in all of them, no conclusion could be drawn as to the frequency of myometrial involvement. In none of those which were fully investigated was there any evidence of gross uterine body involvement, nor of tuberculous disease of the cervix. As in the case of other writers, most of them were discovered accidentally at hysterectomy, by curettage for therapeutic or diagnostic purposes, by uterine biopsy, or some other investigation subsequent to bilateral salpingectomy

Several patients suffering from tubercular endometritis in the series of cases under

review needed hysterectomy some months after the preliminary salpingectomy because of the persistence of discharges and menstrual irregularities. Other patients are known to be still alive and well although active tuberculous disease of the uterus continues. In general, it is felt that no great service is rendered to any patient by bilateral salpingectomy alone when the uterus is also the site of tuberculous disease since a potential focus thus remains which may lead to more serious and generalized complications. The uterus when infected may, furthermore, cause complaints such as backache, discharge and haemorrhage, subsequently necessitating a further operation

Whatever plea may be made for conservation of a healthy uterus, such discrimination is misplaced when dealing with an organ which is unhealthy and, through sterility, functionless. This point is, however, open to criticism as many gynaecologists maintain that menstruation and its associated phenomena are essential for the continued health and well-being of a woman. When such a decision is under consideration it would be well to place all the facts of the case before the patient herself, in advance, so that her permission could be obtained to perform the more extensive operation should this be necessary

Total hysterectomy with bilateral salpingectomy and, if necessary, unilateral or partial removal of the infected ovary, should always be considered a necessary possibility in such cases, provided that the operator has the necessary experience and skill, and that the extent and density of the adhesions do not render the procedure too hazardous

Several cases in the series were examples of generalized peritoneal tuberculosis with but slight tubal involvement. All these patients were treated by the usual complete removal of both tubes and the author reports uniformly satisfactory, immediate

and late results without complication or spread of the disease. This seems to be in agreement with the experience of other operators as reported in the literature, and less doubt appears to exist for the outcome of such cases when treated thus than when treated by either conservative and medical means or irradiation.

It is essential that an operation should not be undertaken without careful exclusion of any active lung tuberculosis. Such a focus deserves to be considered of prime importance and, if overlooked, may be greatly worsened by any operation. It appears wrong to send cases *suspected* of pelvic tuberculosis to a Sanatorium for treatment, although the lungs may be quite healthy. This is surely an unwise step, but one which often occurs.

Dr Dockeray, Pathologist to the Rotunda Hospital, reports that he has seen only 16 such cases in the last 1,515 endometrial specimens examined consecutively from all types of cases in the Rotunda Hospital—an incidence of slightly less than 1 per cent.

COMMENTARY

Of the 15 cases of tuberculous disease of the female genital tract encountered clinically, the following points appear worthy of comment.

Age This averages out at 27 years but, of course, the disease had been in existence for some time before it was detected.

Marriage Seven were married women. Of these 2 had been married less than 6 months, and in these moderately acute symptoms had led to their investigation. The remaining 5 patients had been married for at least 2 years, but mostly 4 to 5 years, before the diagnosis had been established. Of these there were 2 parous women who had full time babies 13 months and nearly 3 years previously.

Symptoms Sterility, transient menorrhagia and other menstrual disturbances, constant lower abdominal pain, with or without backache, and leucorrhoea are the most constant features. Persistent amenorrhoea or menorrhagia were not present nor was there any one constant symptom nor combination of symptoms.

Preoperative diagnosis Only 4 correct preoperative diagnosis were made.

Operation Except where there were troublesome symptoms from *uterine* involvement either before or after the primary operation, bilateral salpingectomy was usually performed with success and satisfactory after results. The ovaries were conserved whenever possible and hysterectomy only employed later when necessary.

Pathological Reports Confirmed the diagnosis.

Primary Focus Contrary to the experience of others this series, from the clinical standpoint, shows that only 3 of the 15 confirmed cases exhibited any primary focus although every effort was made to detect it either pre or postoperatively. This is very definitely opposite to the general opinion.

Sites of the Disease There were no instances of tuberculous cervicitis, vaginitis nor Bartholinitis. Tuberculous salpingitis was more frequent than any other, next most frequently found was involvement of one or both ovaries, while tuberculous endometritis was placed third.

Results All patients continue to enjoy good health without immediate or late complication, if sterility be excluded, whether treated by conservative or more radical surgery (salpingectomy with or without unilateral oophorectomy and/or hysterectomy). This proves nothing but is strongly in favour of the surgical treatment of the condition. In no instance has remaining tuberculous endometritis nor proven tuberculous salpingitis been found to coexist.

with pregnancy in either site. In view of this and the serious nature of the disease it is felt that all patients suffering from tuberculous endometritis should be treated by total hysterectomy with bilateral salpingectomy to avoid further complications.

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The Clinical Significance of the Degree of Calcification of the Placenta as Demonstrated by X-Ray Photography

BY

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DURING the past few years great interest has been taken in the study of placental pathology. This work has, however, served chiefly to emphasize how little is known of the clinical significance of many conditions of the placenta. A few reports, for example, have dealt with the calcium content of the placenta. It has been investigated by biochemical methods by Hegar and Langhans¹ and Wehefritz,² by histological methods by Brehm,³ Ballantyre and Brown,⁴ and by Schonig,⁵ and Masters and Clayton⁶ have shown that the degree of calcification can be determined as reliably by an X-ray photograph of the placenta as by direct chemical analysis.

Wehefritz estimated in 21 cases, 3 to 10 months pregnant, the amount of calcium varied between 0.5 per cent and 4.2 per cent. Ten of his 21 patients were over 7 months pregnant and the calcium content of their placenta showed a tendency to decrease as term approached and then to increase again when postmaturity occurred.

This sinking in the calcium content in the placenta coincides with the time when the calcium requirements of the growing embryo are increased. An interesting parallel to this is the finding by Kehrer⁷ and by V. Wesselow⁸ that the calcium in the maternal blood also decreases slightly in the later months of pregnancy. Beyond such reports little investigation seems to have been attempted of the relation of various clinical features to the degree of calcification of the placenta. It was, therefore, con-

sidered desirable to compare the clinical histories of a consecutive series of 200 of my patients and their newborn infants with the state of calcification of the placenta as judged by postpartum X-ray examination.

The importance of this group of patients for this purpose was greatly increased by the fact that 100 of the 200 patients had been given, from the 26th week onwards, adequate supplementary amounts of vitamins A, B, C and D and of calcium, iron and iodine, manganese and copper, in addition to their diet.

The patients who had been selected for receipt of these accessory substances were a consecutive group taken from a series of patients co-operating in an investigation of the "Nutrition of Expectant and Nursing Mothers in relation to Maternal Mortality and Morbidity" by a Committee selected by the People's League of Health.*

In the series of 200 patients the variation in the number and distribution of the calcareous deposits was remarkable. In 26 per cent of the placentae the X-ray photographs did not show any calcification.

In another 29.5 per cent the amount of calcium seen was very small, showing as a few scattered small calcareous deposits. In 9 per cent calcification was very marked, the deposits being numerous, of varying size, and diffusely distributed throughout

* See Interim Report in *The Lancet* 1942 July 4 10

the area of the placenta. The photographs showed a tendency to increased calcification towards the periphery of the placenta and on the course of the septa.

In order to investigate the clinical significance of the degree of calcification the placentae were arranged in 3 groups, namely those without any calcification, those showing slight, and those with marked calcification. The distribution of cases was, however, almost continuous. Each group included some placentae containing an amount of calcareous deposit approximating quite closely to some members in the adjacent groups.

Figures I and II show typical specimens of calcification.

The distribution of the patients within these 3 groups proved to be as shown in the table below. (The patients who received the supplement of accessory substances to their diet are called treated patients and the remaining half the control patients.)

Calcification of placenta	Percentage of patients		
	Total	Treated	Controls
None	26	21	31
Slight	49	51	47
Marked	25	28	22

Thus nearly half of the total small series was found in the group showing slight calcification of the placenta.

There was evidence of some relation between the treatment given and the degree of calcification of the placenta ($C=+0.12$)*.

The supplementing of the mothers' diet resulted in a decrease in the number of placentae without any calcification and an increase in the number of those showing a moderate and marked degree of calcification as judged by X-ray examination.

In order to estimate the clinical significance of the variations in the degree of calcification of the placenta the following factors in the history of the (A) pregnancy, (B) labour and (C) early puerperium were compared in the groups of patients and their children without any calcification, in those showing slight calcification and in those showing placental calcification.

(A)

- 1 The age of the mother
- 2 The presence or absence of dental caries identified upon their first antenatal visit
- 3 The occurrence of the complaint of oedema
- 4 The duration of gestation

(B)

- 1 The duration of the 1st and 2nd stages of labour
- 2 The efficiency of the 3rd stage of labour

(C)

- 1 The sex of the infant
- 2 The weight of the infant at birth and on the 8th day
- 3 The occurrence of transient difficulty in the act of suckling
- 4 The occurrence of transient icterus neonatorum
- 5 The sufficiency of the milk supply
- 6 The incidence of still births and neonatal deaths

A 1 The degree of calcification of the placenta as judged by X-ray examination does not vary directly with the age of the patient, being most marked in patients between the ages of 25 and 29 and least in those below 19 and over 35 years. The quantitative analysis by Wehefritz of the calcium content of 21 placentae also showed that it bore no relation to the age of the patient.

2 There was only a very slight relation between the presence of dental caries identified upon their first antenatal visit and the degree of calcification shown by the placenta ($C=+0.08$). Twenty-nine per cent of those with caries did not have any calcifi-

* (Estimation of correlations in this paper have been made by using the formulae of Pearson's coefficient of contingency (C) or Yule's coefficient of colligation (W).)



MARKED

FIG 2
Marked calcification

cation of the placenta and 54 per cent of those without calcification did not show any caries (as compared with 63 per cent and 61 per cent in the groups with slight or marked calcification)

3 There was some relation between the development of *oedema* and the degree of calcification of the placenta—more cases of *oedema* being found proportionately among those without any calcification ($C = +20$) There was no appreciable difference in the frequency of the occurrence of this complaint between the treated and control groups of patients having approximately the same degree of calcification of the placenta ($W = -0.07$)

4 When patients having approximately an equal amount of calcification of the placenta were compared the administration of an adequate supplement of accessory substances to the diet did not appear to influence the *duration of the gestation* as judged by the antenatal examinations

The percentage of premature labours was greatest in the group without any calcification, but the number did not seem to vary with the degree of calcification of the placenta. It was almost equal in the groups with slight and marked calcification

B 1 There was no evidence that the treatment modified significantly the *duration of the labour* of the primiparous patients grouped according to the degree of calcification of the placenta nor that the average of either group differed significantly from that of the total group or from that of an unselected series of 1400 consecutive primiparae delivered under my supervision from January, 1935, to December, 1937 (Spiller⁸)

The duration of labour was significantly longer in those patients whose placentae showed the greater degrees of calcification. This may be partly explained by the fact that the greater the degree of calcification of the placenta the smaller the proportion

of babies weighing under 6 pounds and by the fact that the proportion of babies weighing over 8 pounds is higher in the group of patients with excessively calcified placentae

2 It is of interest to try to estimate whether the degree of calcification of the placenta had any influence on its *separation* and *expulsion* from the uterus

This can be gauged to some extent by a study of the frequency of manual removal of the placenta and of the incidence and degree of excessive loss of blood before and after the completion of the third stage

In 2 cases out of 200 patients (both of them control patients) manual removal of the placenta was necessary. One of these placentae showed only very slight calcification and the other slightly more calcification. The loss of blood was slightly excessive in 4 per cent of the control cases but in none of the treated cases. In 1 per cent of the cases the loss of blood was more excessive. There was no evidence that the occurrence and degree of this haemorrhage bore any relation to the degree of calcification of the placenta

C 1 The degree of calcification of the placenta was not related to the *sex* of the child. In the group of placentae without any calcification the child was female in 59 per cent of the cases. In the group of the placentae with a slight and an excessive amount of calcification the two sexes were approximately equally numerous. This may be compared with the analysis by Wehefritz of 21 placentae which also showed that the degree of calcification of the placenta did not vary with the sex of the infant

2 The amount of calcification shows some relation to the *weight* of the infant (Control $C = +0.26$ Treated $C = +0.18$). The greater the degree of calcification of the placenta the smaller the proportion of babies weighing under 6 pounds. On the

other hand the proportion of babies weighing over 8 pounds was higher in the group of patients with excessively calcified placentae than in the groups with a moderate degree or no calcification

It was not surprising to note that a larger proportion of the babies weighing less than 8 pounds were female than were male, and that on the other hand the males predominated among the babies weighing 8 pounds and over. When a comparison was made between the male and female babies not only as to the degree of calcification of their placentae but as to the relation of this to their weight some interesting details were obtained

Approximately half of the male and of the female babies weighing between 6 and 8 pounds had placentae showing a moderate degree of calcification. Yet no calcification of the placenta was more frequent in the few male infants weighing under 5 pounds and marked calcification was more frequent among the female babies weighing over 8 pounds. Whatever amount of calcification was present in the placenta the degree of preponderance of the female sex over the male varied inversely with the weight. The difference of weight between the birth weight and that on the 8th day did not vary with the amount of calcium seen in the placenta. There was no evidence that there is any difference of significance between the change in weight of the child of the treated and untreated mother having approximately the same amount of calcium in the placenta

The difference between the weight of the child at birth and on the 8th day did not vary with the birth weight of the baby which showed some relation with the amount of calcium seen in the placenta

3 Minor degrees of transient difficulty in the act of suckling were present in 12 per cent of the babies. Almost half of these babies had had placenta without any calci-

fication. No difficulty in suckling was noted in the group in which calcification was most marked. There seemed evidence that there is some relation between the frequency of the occurrence of difficulty in suckling in a group of babies and the amount of calcification demonstrated in the placentae of that group ($C = +0.16$) but none is shown between the supplementary diet given to the mother during the later weeks of pregnancy and difficulty in suckling ($W = -0.09$). This relation is paralleled by that found to exist between the birth weight of the child and the degree of calcification of its placenta

4 *Transient icterus neonatorum* occurred in 8 per cent of the babies. This condition was most prevalent among the infants of the group of patients without any calcification of the placenta and absent in the group of those having the most marked calcification. There seemed evidence of a very slight relation between the two conditions ($C = +0.07$) but there was not sufficient evidence to indicate a relation between the supplementary diet given to the mothers in pregnancy and the incidence of transient icterus neonatorum ($W = +0.02$)

5 Eleven per cent of the untreated patients were unable to completely feed their babies and 14 per cent of the treated women were unable to feed their babies completely. In both the untreated and treated groups the failure to feed completely the baby was most frequent among the groups of women showing a moderate degree of calcification of the placenta

Failure to supply completely the baby with milk was about equally frequent among the group of women without any calcification of the placenta and that having marked calcification

The percentage of mothers unable to supply sufficient milk upon discharge from hospital did not vary with the amount of calcium present in the placenta ($C = 0$)

6 No relation was found between the

incidence of *still births* and *neonatal births* and the degree of calcification of the placenta as judged by X-ray examination

SUMMARY AND CONCLUSIONS

1 Approximately half of a small series of 200 placentae examined by X-ray showed a moderate degree of calcification

2 There was some evidence that the supplementing of the mother's diet with calcium and vitamins resulted in a decrease in the number of placenta without any calcification and an increase in the number of those showing a moderate and marked degree of calcification

3 Some relation was demonstrated between the degree of calcification of the placenta and (1) the absence of dental caries as noted at the first antenatal visit, (2) the absence of a complaint of oedema, (3) the duration of labour, (4) the birth weight of the infant, (5) the absence of transient difficulty in the act of suckling, (6) the absence of transient icterus neonatorum

4 The amount of calcium seen in the placenta did not appear to vary with the age of the mother nor with the sex of the infant

5 The degree of calcification of the placenta was not related with the duration of the gestation, the efficiency of the 3rd stage of labour, the change in weight of the infant by the 8th day, the sufficiency of the milk supply and the incidence of still-births and neonatal deaths

6 In the patients grouped according to the degree of calcification of the placenta no significant difference in the presence of

oedema of the feet and ankles, the duration of gestation, the duration of labour, the change in weight of the infant by the 8th day, the occurrence of transient difficulty in suckling, the occurrence of transient icterus neonatorum, was found when the treated and control patients were compared

I thank Dr E. Ulysses Williams and his staff for the X-ray photography and the People's League of Health and Miss Olga Nethersole for securing the free gifts of the vitamin and mineral elements from Messrs Crookes Laboratories, Roche Products Limited and Vitamins Ltd

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Traction on the Groin in Breech Presentation

BY

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IN 1686 Mauriceau in his famous "*Traite des maladies des femmes grosses*" mentions traction on the presenting breech by one forefinger slipped over the foetal groin from the outer side, or by both forefingers slipped over both groins. I shall use the term "Mauriceau's grip" because the term "Mauriceau-manoeuvre" is generally used with reference to his method of extracting the aftercoming head. In the eighteenth century Pan and Smellie recommended traction by a fillet slipped over the groin, or by a blunt hook. Since then generations of authors have suggested improvements—up to Bunge's carrier and Kuestlin's hook—a sure sign that all methods have some disadvantage.

Disadvantages Only limited force can be exerted by finger traction. It has been recommended that this force might be increased by grasping the wrist of the operating hand with the other hand. But even this is sometimes insufficient. Traction by the fillet and by the hook can be much stronger, but the possibility of injury to the foetus and to the mother is then increased, the hook has, indeed, been described as "not an instrument, but almost a weapon." The risk of injury to the foetal bones is great unless the force is applied by the finger.

This applies to the normal mature 9 months foetus, but may not be so in the case of children who are weak or immature and have delicate bones and cartilages. The more immature the baby, the greater the

risk, and even infants at term may occasionally have delicate bones calling for caution. It is often said that injuries to the femur may be prevented if the finger, or the instrument, is pressed backwards during the traction against the foetal trunk to avoid any pressure on the thigh-bone or hip-joint, but I wish to draw attention to the possibility that even then, damage may be caused to the delicate foetus.

Anatomical Conditions An unexperienced student is easily misled by comparing anatomical conditions of older babies with those of a new-born child. There is only one part of the groin strong enough to stand a heavy pressure, i.e. the cental bulk of the partly ossified innominate bone, where the os pubis and the os ischi meet the ilium, and where there is a strengthening from below by the hip-joint. In older children pressure on the groin from above meets only an elastic mass consisting of the ligamentum inguinale, and of muscle insertions, principally the sartorius and the tensor fasciae latae. This area spreads from the upper interior spine of the ilium in a distal and medial direction, offering a solid resistance. In new-born children, however, this elastic mass is not yet developed, the muscles are weak and the ligamentum inguinale is only slightly demarcated by some tender fibres. It develops much later from the tendinous insertions of the musculus obliquus and other muscles. Thus any pressure from above will be directed straight on to the bone.



Fig 1

Breech presentation Minceur's grip Finger pressure on the chest

M W



Fig 4

Breech presentation Finger lifting, passed between the thighs as pressure on the central bulk of the innominate bone

M W

Now in Mauriceau's grip it is not the central mass of the innominate bone that meets the pressure, between the finger of the operator and the central bulk lies the upper part of the ilium. Figs 1, 2 and 3 demonstrate this relation of the operating

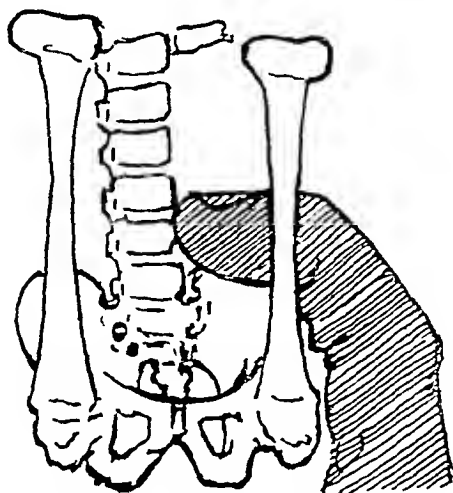


FIG 2
Traction on presenting breech by
the Mauriceau grip

finger to the foetal skeleton. In a vain attempt to enter the groin, the forefinger in Fig 1 passed over the iliac crest of a new-born child with flexed thighs. Fig 2 shows the same error illustrated with the aid of a foetal skeleton. The lateral aspect of the left innominate bone in Fig 3 shows clearly that a finger could not be squeezed in the narrow gap between the anterior superior spine and the femur. The whole pressure of the finger has to be borne by the thin lamella of the partly-ossified iliac cartilage. When the operator in Mauriceau's grip ignores the advice to make the traction only against the foetal trunk, the finger slips easily along the iliac crest to the thigh, presses on the shaft of the femur and the bone may be broken. This lever action is a source of great danger to the femur. It may seem of value to slip a thin fillet such

as a catheter or a fold of gauze in the gap between the anterior superior iliac spine and the thigh. But then the danger is merely transferred from the iliac bone to the hip-joint, violent force threatens the soft part with cuts, the hip-joint with dislocation and the neck of the femur with fracture. With a broader fillet, or hook, the menace to the ilium is the same as in Mauriceau's grip or even increased, inasmuch as one misses the touch of the finger to decide the line of pull.

Experiments have shown that in the normal child at term, not only the bony part of the ilium but also its non-ossified cartilaginous part can withstand heavy repeated

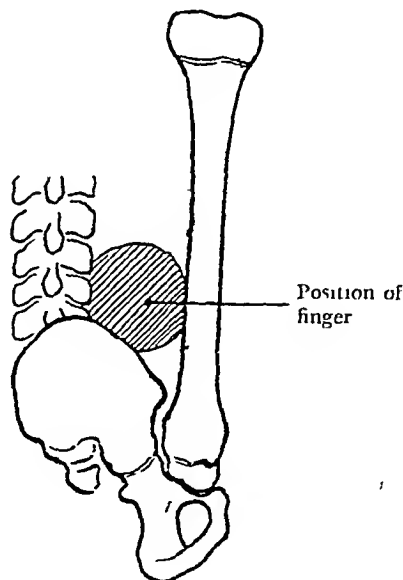


FIG 3
Lateral aspect on pelvic part of foetal skeleton
with flexed femur in presenting breech. Position
of forefinger in Mauriceau's grip

pressure by Mauriceau's grip. In the case of poorly ossified or premature foetus the upper iliac lamella is too thin to stand the required pressure at its crest, and a serious injury of the upper part of the ilium is, therefore, possible. While the obstetrician

can easily detect a fracture of a femur, he may overlook damage to the ilium if he does not keep such a possibility in mind. I

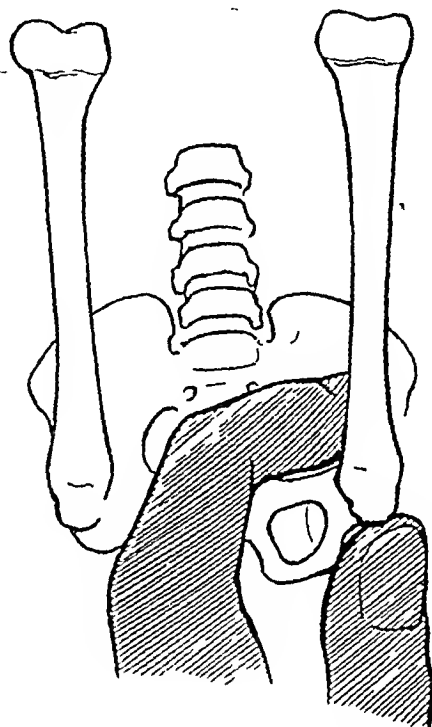


FIG 5
Suggested modification of traction in presenting breech

am not aware that such damage has been reported, but I have myself seen it. In Central Europe from 1917 a very large percentage of new-born children had retarded ossification, certainly due to under-nourishment of the mothers. So far as I have been able to observe, the average condition of the bones of children in Hertfordshire, where I am at present living, is better than that of children in Central Europe—not to mention India. When heavy traction has been used to deliver such a delicate foetus a later examination of the ilium by X-rays would be advisable.

If unilateral injury to the pelvis has taken place an oblique deformity may later

develop. It would be a matter of interest to investigate this possibility.

A Safer Manoeuvre Led by these considerations I have proposed a different manoeuvre using the right hand for right-sacral positions and the left for left-sacral positions. The forefinger or the middle finger should be placed on the foetal groin by passing between the thighs. To prevent the finger from slipping, the operator can strengthen his grip by placing his thumb firmly on the foetal buttock, thus holding the breech between his fingers (Figs 4, 5 and 6).

Disadvantages The greatest disadvantage is that in this form of grip the traction produced with only the first phalanx is

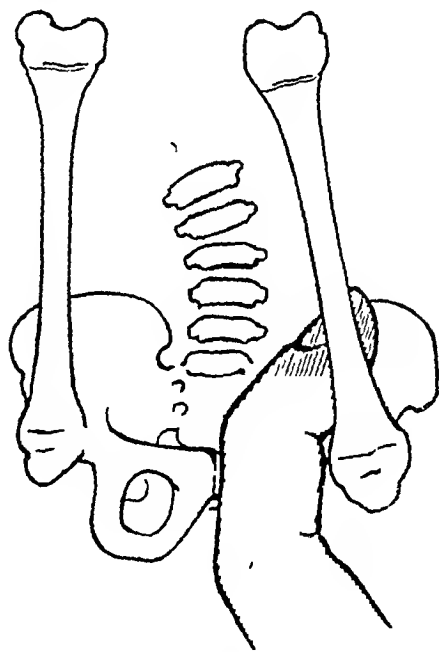


FIG 6
Modified traction alternately on posterior and anterior groin by supination and pronation on the operating (right) hand

even weaker than can be obtained in Mauriceau's grip. The ability to produce a rotation by pressure on the groin is at

least the same as in the case of Mauriceau's grip

Advantages The chief advantage is the increased safety when dealing with an immature or weak child. The pressure is exerted directly on the central bulk of the innominate bone from the most accessible direction. Dangerous pressure at the iliac crest is avoided. If the operator wishes to exert a more effective traction then he can produce with his first phalanx, he can push the finger high up over the groin. In this way the force of traction is equal to that of Mauriceau's grip, especially when the operator succeeds by lateral traction in bringing the upper ilium to a more horizontal position (Fig 6). Further, by repeated pronation and supination of the hand the operator can exert traction on the anterior and posterior groins alternately. By this means a portion of the foetus is moved at one time and friction resistance is correspondingly lessened. This greater freedom to push and pull in various directions helps to direct the progress along the pelvic axis.

When more force is essential, and when there is room, I suggested in 1922 the

use of both hands. Rubeska, Professor Mueller's assistant, published some years later 5 cases from the University Hospital in Brno, Czechoslovakia, where he had tried in vain in frank breech presentation to finish the extraction by every other method. He finished the extraction successfully by placing, after my previous suggestion, one forefinger over the groin from inside, and the other from outside over the groin till both came in contact.

CONCLUSION

When a premature foetus, or a foetus with retarded ossification has to be delivered by the breech, injury to the bones may be caused by the usual methods of traction. A manoeuvre is described by which delivery may be more safely accomplished.

I wish to express my sincere thanks to Professor Chassar Moir for his kind readiness to provide facilities for testing my suppositions by dissections at the Nuffield Department of Obstetrics and Gynaecology in Oxford.

Haemangioma of Arm Causing Delay in Delivery and Neonatal Death

BY

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ALTHOUGH tumours of the blood vessels are said to be the most common type of neoplasm occurring in infancy the record of an unusual case may be of interest

Baby C.T., the second child of a healthy mother was born after a labour of $4\frac{1}{2}$ hours, which was normal up to delivery of the head. After birth of the head there was delay in advance though the uterine contractions were satisfactory. Examination failed to reveal unduly large shoulders and eventually by manipulation the shoulders were delivered and the child's arms freed, revealing the cause of delay.

The baby, a well developed male child, weighed 8 pounds, length $22\frac{1}{4}$ inches, head circumference $14\frac{1}{2}$ inches. The left arm was the site of a tense cystic swelling 9 inches in circumference and extending from $1\frac{1}{4}$ inches above the wrist to $1\frac{1}{2}$ inches below the acromion. The overlying skin was extremely congested and mottled.

In the nipple line over the axillary border of the pectoral muscles of the same side was a vascular swelling about the size of half a walnut. A thrill could be felt over this area, and on auscultation a loud bruit was heard. There was no cardiac murmur.

Movement of fingers and wrist of the left hand was good, but elbow movement was limited by the size of the arm in that region, and complete extension was impossible. The tumour appeared to be of vascular origin.

On the day after birth the child suffered from cyanotic attacks, and the affected arm became more swollen. Cyanosis increased, the lower extremities and right arm appear-

ing almost black during the attacks. In spite of protective dressing and support, superficial areas of necrosis developed in the region of the left elbow. Death took place on the 3rd day, postmortem staining being intense and rapid of onset.

Postmortem

Dissection of the left arm showed that the tumour originated in the superficial tissues. The muscles and bones being normal. The subcutaneous tissues in the region of the swelling were the site of oedema and extreme congestion, fluid oozing out freely on incision. Large varicose vessels ramified throughout the area, and dilated and hypertrophied vessels were traced to the axilla.

On opening the thorax a greatly enlarged heart presented. The pericardium contained a considerable amount of fluid, and the heart was dilated to about three times its normal size. The cardiac muscle appeared normal. Both lungs were poorly expanded but otherwise normal. Nor was any other abnormality found.

Pathological Report on Tissue from Arm

A cavernous haemangioma characterized by an unusual degree of haemorrhage into the rather loose myxomatous matrix.

At one margin of the tumour a small bundle of rather embryonic-looking striped muscle appears to be involved in the angiomatous process. The cells of the vascular spaces are lined by a single layer of simple flattened endothelium and the spaces themselves vary from capillary to

cavernous size There is nowhere any suggestion of malignancy

DISCUSSION

The case under discussion presents two points of special interest First, there is delayed delivery due to the great size of the affected arm Secondly, neonatal death resulted from cardiac failure due to dilation of the heart in response to the mechanical obstruction to circulation offered by a simple vascular tumour of arm

While the foetus was *in utero*, and the maternal circulation functioning, the foetal vascular system felt no added strain from the presence of the tumour, but once separate existence was established the obstruction became severe, resulting in cardiac dilation with its associated cyanosis

According to Muir,¹ the haemangioma is a mass of blood vessels atypical or irregular in arrangement and size, and to be regarded as abnormality in growth rather than a true tumour Although often ill-defined at the margins it is essentially of simple nature

A few instances have been recorded in which angiomas have formed numerous metastases and yet have presented the histological features of comparatively simple growth

Rambar,² in an article on "Angiomas in premature infants," remarks on the frequent occurrence of this type of tumour and quotes several theories of causation

Unna³ considers the condition to be due to abnormal pressure in foetal life, while Ribbert⁴ states that angiomas develop from embryonic rudiments Virchow's⁵ theory is that the growth results from the action of local irritation on imperfectly-formed vessels, as those found in embryonal fissures According to Ewing,⁶ origin lies in a developmental anomaly in the structure of certain vascular segments which retain embryonic characters

Jenkins and Delaney⁷ reporting a series of 256 cases of angioma also deal with the theories of origin, and quote Rokitsansky as stating that the tumour arises from simple hypertrophy, not neoplastic overgrowth of vascular segments, while Lowenthal regards trauma as an important factor

In their review of the series of cases Jenkins and Delaney state that "An hereditary influence does not appear to play any role" In view of this statement it is interesting to note that the sister of the baby under discussion has a haemangioma the size of a florin below the left clavicle

Mahner⁸ in 1936 reported an "Unusual Extra Cardiac Murmur Simulating Organic Heart Disease"—a haemangioma of abdominal wall, by obstruction the normal flow of blood giving rise to a murmur in the vicinity of the precordium

SUMMARY

A case of haemangioma of the arm is described

The tumour was of sufficient size to delay delivery, and the mechanical obstruction to circulation such, that death from cardiac failure resulted on the 3rd day

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Uterus Didelphys

BY

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A CASE OF NORMAL DELIVERY IN UTERUS DIDELPHYS AFTER A PREVIOUS CAESAREAN SECTION

CASE NOTES

Mrs. E. C., 2-para, aged 29 years, was first seen on December 9th, 1940. She was in excellent health. Her last menstrual period was on August 7th, 1940, and thus the expected date of delivery was May 14th, 1941.

Menstrual History Periods always regular Type 7/28 days Loss Very heavy

PREVIOUS HISTORY

During her first pregnancy the patient attended Nottingham Hospital for Women and the following summary of her case was obtained:

"This patient attended the hospital in May 1937, and was admitted in July. She had a septate vagina and double uterus. Pregnancy was in the left uterus, the right one lying below it and filling up the pelvis.

"At term she was admitted and under anaesthesia an attempt was made to push up the right uterus out of the pelvis. This was impossible so a lower segment Caesarean section was performed. The right uterus was then pulled up and the round ligament on that side plicated. She was seen 3 months later when it was noted that the position of the right uterus was considerably improved. The child weighed 6½ pounds.

VARYING degrees of abnormality occur in the genital tract, all being due to the non-union of the Muellerian ducts. If the two Muellerian ducts fail to fuse along the whole of their lengths, and if they develop normally and remain separate, a condition which is termed uterus didelphys results. This extreme degree of maldevelopment is usually associated with gross errors of development in other parts of the body, so that it is rare to meet the condition in adults. In uterus didelphys, the two vaginas open at the vulva where a vaginal septum can be seen. A cervix lies at the top of each vagina, and the two parts of the uterus above the level of the cervixes are completely separate.

Palmer Findly states that patients with uterus didelphys are unusually fertile and may menstruate during pregnancy, from the non-pregnant side of the uterus duplex. During pregnancy the non-pregnant uterus develops a decidua, which is discarded with the lochia in the puerperium.

Smith and Straussmann point out that uterus duplex predisposes to abortion and premature labour. The non-pregnant uterus may obstruct the passage of the child during labour.

Both uteri may become pregnant at the same time and give rise to twins, or conception may take place at different times, and this may be the explanation of twins born at different dates.

PRESENT CONDITION

The patient was a very healthy woman with no obvious congenital defects. The heart and lungs were normal. The blood-pressure 128/74 and the urine clear. On examination of the abdomen the uterus was seen to be lying obliquely to the right and enlarged to the size of a 16 weeks' pregnancy. On vaginal examination a well-marked vaginal septum was present, with a cervix at the top of each vagina. Both cervixes were soft, the pregnancy being in the right uterus this time. The patient was seen at regular intervals during the pregnancy and remained very well. At 36 weeks the presentation was a breech and the left uterus was just palpable at the symphysis pubis. Gentle external version was attempted, but was unsuccessful as the breech was engaging in a roomy pelvis.

The patient was admitted to hospital in labour on May 11, 1941, at 8 o p m. The membranes ruptured at 8 50 p m and vaginal examination at this stage disclosed the right cervix dilated to the size of a two-shilling piece. The left cervix was soft and patulous. Both uteri could be felt contracting rhythmically. Labour progressed normally and at 2 30 a m on May 12th, the cervix was fully dilated with the buttocks presenting at the perineum. The patient delivered herself easily with little assistance. The posterior attachment of the vaginal septum was torn and a small first degree perineal tear sustained. The tear was sutured. The 3rd stage was normal, both uteri being clearly defined and well contracted. The child was a girl and weighed 7 pounds. The puerperium was very satisfactory, on the 4th day a large shaggy decidual cast was passed.

Vaginal examination on the 12th day of the puerperium disclosed a well-healed perineum and both uteri involuted in an anteverted position.

DESCRIPTION OF THE DECIDUAL CAST

The expelled cast from the non-pregnant cornu or half of the uterus is an elongated hollow finger-like structure about $5\frac{1}{2}$ inches in length by $1\frac{3}{4}$ inches broad, while it is open at one extremity—the upper—and closed at the lower end. When first passed it was of a dark reddish colour but after fixation in 4 per cent formalin it became paler. The outer aspect is shaggy and rough where it has been separated from the uterine wall, while the inner surface is smooth and congested and the calibre of this hollow decidual tube just accommodates an ordinary test tube comfortably. The only sign of the cornual projections is an irregular outgrowth on one side of the upper extremity of the cast and thus, together with the fact that the upper extremity of the specimen is open, indicates the probability of the upper end, including the cornual projections, having become separated so that it did not come away with the main specimen.

On microscopical examination the decidua is seen to have a very open general structure owing to the presence of multiple spaces of varying size and shape so that in some fields the appearance is almost trabecular and consists mainly of these spaces with intervening bands of intervening solid tissue of varying thicknesses, while in other fields the structure is more solid but still contains a varying number of spaces. These spaces might justifiably be taken to represent distended glands especially of the spongy layer of the decidua but an epithelial lining is entirely lacking, probably on account of disintegration, only an occasional lining cell is to be seen and these are of a flattened endothelial-like appearance which is probably due to the effects of acinar distension.

The main solid structure is composed of closely-packed polygonal decidual cells with characteristic large nuclei which here

and there show mitotic figures. In many places the protoplasm and the cell boundaries are not very clear thus indicating some degeneration towards the end of pregnancy. Blood vessels are not prominent.

Further examination of patient 6 months after delivery

General Condition Excellent

Menstrual History Regular normal periods

X-ray examination after Lipiodol injection into both uterine cavities on April 26, 1942

Examination at this period showed the vulva to be normal, at the upper end of the vagina a fleshy anteroposterior septum was felt dividing the vault into two cavities. On each side of the septum a cervix was seen indicating a double uterus. Lipiodol 8 c.c. was injected into each uterine cavity and an X-ray examination made (see plate).

I am indebted to Dr. David Rocyn Jones, County Medical Officer, and Professor G. I. Strachan, Consulting Obstetrician, for permission to report this case.



X ray after Lipiodal injection into both uterine cavities

N K

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

The Quarterly Meeting of the Council was held in the College House on Saturday, January 30th, 1943, with the President, Sir William Fletcher Shaw, in the Chair

The following candidates were elected to the Membership of the College —

Janet Elizabeth Bottomley, London

Phyllis Dingle, London

Marjone Olive Dunster, Bristol

Christina McDonald McTaggart, Edinburgh

Louis Resnick Cape Town, South Africa

Gordon Short Sturtridge, Melbourne, Australia

Kenneth Gordon Patrick Worner, Melbourne,
Australia

Review of Current Literature

Director: FREDERICK ROQUES M A , M D , M Chir (Cantab), F R C S , F R C O G

THIS Review contains the lists of contents and abstracts of the more important articles from the journals with which the *Journal of Obstetrics and Gynaecology of the British Empire* exchanges

The Review of Current Literature has kept the readers of the Journal in touch with current literature throughout the world owing to the war many

journals with which the *Journal of Obstetrics and Gynaecology* previously exchanged are no longer received At the end of the year an Index of all the subjects contained in the articles of the journals reviewed is printed Arrangements are also made to include abstracts of important articles on borderline subjects such as Physiology Biology, and Biochemistry

LIST OF ABSTRACTORS

J LYLE CAMERON F R C S
W E CROWTHER, M B
R H B ADAMSON, M D
B JEAFFRESON, F R C S

P MALPAS, F R C S
T N A JEFFCOATE F R C S
MEAVE KENNY, F R C S
JANE H FILSHILL

The Lancet

July 14th, 1942

*Hospital or domiciliary confinement Mathilda F Menzies

July 18th 1942

*Influence of thyrotoxicosis on menstruation P M G Russell and Edna M Dean

August 1st 1942

The onset of respiration at birth Sir Joseph Barcroft

August 15th, 1942

*Development of hypochromic anaemia during pregnancy H A Hamilton Helen P Wright

August 22nd, 1942

*Three cases of locked twins S W Wright

September 19th 1942

Pernicious anaemia of pregnancy H G Miller, and T C Studdert

HOSPITAL OR DOMICILIARY CONFINEMENT

The author reports that in Leyton in the last 10 years there has been a noticeable decrease in domiciliary births with an increase in institutional births 1940 was the only year which showed an

increase in delivery at home on the preceding year On investigating the cases the number of abnormalities was found to be much higher in hospital than in domiciliary work The percentage of abnormalities showed a rising figure from the youngest to the oldest age-group and it was evident that a larger proportion of the older primiparae should be admitted to hospital, if a medical discrimination had to be made Instrumental deliveries were seven times more frequent in primiparae than in multiparae and their frequency was related to the age of the primipara being needed much more often in patients between 35 and 40 years of age Toxaemia was twice as common in primiparae as in multiparae and the risk appeared to be nearly as great in the younger age-group as in the older On following up the breast feeding of the infants the most striking difference between the hospital and domiciliary cases was the increase of 10 per cent in the hospital group in the number of babies who were artificially fed within two weeks of birth

The author also discusses the reasons why in

her opinion, admission to hospital has become so popular. The commonest argument advanced by the mother was lack of adequate accommodation at home. In 1940 the accommodation was no better than in previous years in fact it was probably worse from over-crowding so this reason was obviously incorrect. It is pointed out that the difference in the distribution of hospital and domiciliary births in 1939 and 1940 was essentially the result of the mother's being advised in 1940 where to have her confinement instead of as in 1939 making the choice herself. Cost was probably the first thing most mothers consider and secondly the fear of pregnancy and labour. The author is of the opinion that admission to hospital and the prominence given to the subject of maternal mortality is liable to produce a distorted view in the mind of the mother. She also feels that the insistence on the necessity for antenatal supervision may have the unfortunate effect of making women feel that there must be something wrong with them instead of engendering confidence in their capacity to bear children normally. She says that hospital confinements certainly surround childbearing with an atmosphere of abnormality. Although three out of four women may have had normal labours by the end of the fortnight there is probably little they do not know of the sufferings of the fourth and then they can hardly fail to be influenced by what might have happened to them. The author also says that the woman who accepts childbearing and looks forward to it is more likely to have several children than the woman who is full of fears therefore it may be that increasing confinement in hospital has effects inimical to childbearing which are not obvious from studies of maternal mortality.

INFLUENCE OF THYROTOXICOSIS ON MENSTRUATION

There is a divergence of opinion on the effect of thyrotoxicosis on menstruation. The bald statement that it tends to produce haemorrhagia is found in the common English textbooks whereas in this reported series of 130 cases it was present only in 2 cases. The authors studied these cases not only to find out the effects of thyrotoxicosis on menstruation but also the effects of thyroidectomy on the menstrual periods. Patients at puberty or the menopause those with a history of recent delivery or abortion or those who had recently

undergone a gynaecological operation were not included in the series. These 130 cases were divided into severe (29), moderate (70), and mild (40) types. Menorrhagia was present only in two of the moderate group. From a study of all these cases it became evident that in mild cases and probably therefore, in the early stages of the disease there is no effect on the periods as the condition progresses there is an increased tendency towards scanty and irregular periods and finally more than half the severe cases develop amenorrhoea. Often however the periods are not in any way affected even in severe thyrotoxicosis.

On investigating the results of operation, accurate notes were available in only 79 cases. No alteration in the periods occurred when these were formally normal (40 cases). A return to normal after previous disturbance of the cycle occurred in 30 cases. A persistence of the abnormality occurred in only two cases. The periods became abnormal after being formally normal in 7 cases. Thus there were 39 cases with an abnormal menstrual history among the 79 cases operated on for thyrotoxicosis and of these 30 returned to a normal cycle.

DEVELOPMENT OF HYPOCHROMIC ANAEMIA DURING PREGNANCY: RESPONSE TO IRON THERAPY

Hamilton and Wright present a series of 196 cases of pregnancy anaemia treated with iron therapy with a control series of a similar number of cases. Haemoglobin estimations were carried out by the Haldane method on all the patients attending the antenatal clinic on two days of the week. Iron was administered as ferri et ammonii cit or as pil ferri sulph to all on one of these days while those attending on the other day were used as controls. The average initial haemoglobin estimation was 75 per cent in the group to be treated and 79 per cent in the other group. The average terminal haemoglobin estimation of these two groups was 77 per cent and 70 per cent respectively. Further of those receiving treatment 54 per cent showed an improvement while of the untreated group 13 per cent only improved.

Although it seems that the improvement in the treated cases was not very great the authors are of the opinion that all pregnant women should be given iron medication and a diet rich in iron during

the pregnancy The administration of iron in anaemia usually quickly brings the haemoglobin percentage to a much higher figure than these authors have reported, and, therefore, it seems that there is a deficiency in pregnancy of some other factor which utilises iron

THREE CASES OF LOCKED TWINS

Before describing the details of his 3 cases, the author discusses the various ways in which this complication can occur (a) Both foetus presenting by the vertex, their heads entering the pelvis side by side, (b) first child presenting as a breech and the second as a vertex, chin to chin, (c) both foetus presenting by the breech, the buttocks of the second child entering the brim with the thorax of the first, (d) first child presenting as a breech, becoming locked by the chin on the body of the second lying transversely and (e) both foetus presenting as footlings and entering the brim together Locked twins is said to occur about once in every thousand twin labours, and it is then necessary for the foetus to be small and the pelvis very large

In the first case described by the author, the foetus were locked chin to chin and he had to eviscerate the first breech child and decapitate before he was able to disimpact them In the second case the first child presented as a breech and the head of the second child was extended lying transversely and wedged in between the shoulder and head of the first This abnormality was complicating a severe toxæmia and shock of unknown origin, but under gas and oxygen anaesthesia he was able to disentangle the heads by bringing the occiput of the second head to the front In the third case, both foetus presented as a breech The pelvic brim was occupied anteriorly by the neck of the first child, while behind it the flexed legs and buttocks of the second child had descended just below the level of the brim and fitted into the nape of the neck of the first child Disentanglement was easily carried out by pushing up the lower pole of the second foetus and by pulling down the first foetus so that the head passed into the pelvic cavity Both children were born alive

BRYAN JEAFFRESON

The British Medical Journal

July 25th, 1942

*Intra-uterine infection of foetus by gas gangrene organisms F H Kemp and J A Stallworthy

August 1st, 1942

*Antihormones Editorial

Maternity service of the future G Winn
Everett, Edward A Wilson, R C B Ramsay
and Stephen A Scorer

August 8th, 1942

Parturition with fractured femur G Blundell
Jones

*Simmonds's Disease Annotation

August 15th, 1942

*A maternity service scheme Dame Louise
McIlroy

August 22nd, 1942

*Vaginismus its management and psychogenesis
Joan Malleson

An interesting breech delivery W L Macdonald
September 5th 1942

*An alphabet of breast feeding Charles McNeill
Shock treatment in psychosis complicating pregnancy E T Thorpe

INTRA-UTERINE INFECTION OF FOETUS BY GAS GANGRENE ORGANISMS

The authors describe a case of intra uterine death in which a radiograph revealed gas inside the foetal skull Bacteriological examination after delivery showed the presence of a pure culture of *cl Welchii*

They point out that had a perforation been performed a pure culture of *cl Welchii* would have been released into the genital tract

The infection was apparently limited to the foetal skull and probably was blood-borne through the placenta

ANTIHORMONES

Animals having repeated injections of extracts of endocrine glands from a different species become refractory to the physiological action of these extracts

Some doubt exists as to whether this is due to the formation of antagonistic hormones or true antibodies Owing to the relatively crude preparations of hormones which are available there are always some antigens, such as serum proteins,

present which are characteristic of the species rather than the hormone. Thus any precipitation or complement fixation may be due to these antigens rather than to a direct reaction between the hormonal extracts and the antihormone. The more highly purified the extract which is used for immunization gives, however, smaller amounts of precipitating or complement fixing antibodies.

Many of the physical and chemical properties of antihormones and sites of formation are suggestive of their being true antibodies. Amongst these are precipitation in the globulin fraction of serum, resistance to heat and changes in the hydrogen-ion concentrations and species-specificity.

Final proof as to the nature of antihormones will depend upon the demonstration of an *in vitro* reaction with the corresponding hormones in the test tube. It is likely that the final proof will come in the field of synthetic immunochemistry.

SIMMONDS'S DISEASE

This disease occurs most frequently in women between 30 and 40 years of age, who have borne several children. There is usually a history of trauma or postpartum haemorrhage. The cases are usually fatal and are due to some destructive lesion of the pituitary. Non fatal cases are similar in their clinical picture to other cases of wasting and weakness, especially anorexia nervosa.

Insulin tolerance tests show that the initial fall in blood-sugar after insulin injection is followed by a longer delay in return to previous fasting level in cases of Simmonds's disease. This is also present in some cases of anorexia nervosa.

However, 17-ketosteroid assays are negative in Simmonds's disease but positive in anorexia nervosa.

T. N. A. JEFFCOATE

A MATERNITY SERVICE SCHEME

In her opening remarks at the opening of a discussion at the obstetrical section of the Royal Society of Medicine the speaker referred to the economic aspect of midwifery practice.

She held it to be impossible to separate midwifery from gynaecology as treatment is so frequently required for post-natal complications. Referring to defects in the present maternity services she held that the limited number of maternity beds, especially in industrial areas, was a major defect.

In the future there would tend to be a greater

tendency towards reduction of domiciliary midwifery owing to the difficulties of housing and home service.

Antenatal clinics in connexion with maternity hospital staffs are satisfactory as there is continuity of supervision during pregnancy and childbirth. In county and municipal antenatal clinics the clinical experience may be very little in midwifery and the main qualification for the post of a medical officer may be the possession of a diploma in public health. The want of continuity of treatment between public antenatal clinic, private practitioner and postnatal clinic may lead to unjust and incorrect criticism of work carried out for any given patient. The fault lies in the practice of dual responsibility.

A great debt was owed to voluntary hospitals and organisations in midwifery practice and it was satisfactory to realize that the present Minister of Health proposed to continue to retain the voluntary institutions in his general scheme of medical services.

Reference was made to the decline of midwifery in general practice, partly as a result of an improved midwives' service and partly as a result of a declining birth rate.

It was noted that in Scotland midwifery was more in the hands of the general practitioner than it was in England.

R. H. B. ADAMSON

VAGINISMUS ITS MANAGEMENT AND PSYCHO-GENESIS

There must be many marriages which are not actually consummated and patients are frequently surprised when the position is explained to them.

The author deals mainly with those cases in which the trouble comes mainly from the woman's side.

The syndrome of vaginismus varies from spasm of the perineal muscles to extreme adduction of the thighs with opisthotonus. There is also frequently an area of hyperaesthesia varying in extent. The spasm cannot be voluntarily produced and may appear in spite of desire for intercourse. It can, however, be modified by conscious control.

The author gives a detailed account of the management of these cases which largely entails treatment by persuasion. Examination must be made in the dorsal position as the lateral position

gives more relaxation and thus conceals the severity of the spasm. Because of the excessive modesty present in many of these patients avoidance of visual exposure is a desirable feature. A kindly but firm manner should be adopted during the examination.

Useful adjuncts are the use of non greasy lubricants and a support under the buttocks before sexual intercourse.

In cases in which the hymen remains unstretched the dilatation may be done by the patient herself after instruction or the dilatation may be done under anaesthesia and followed by the use of dilators by the patient herself.

The author has investigated the aetiology of the condition and finds a high percentage of patients have memories of some pelvic trauma. In early childhood. These memories include frequent enemata suppositories and the old-fashioned soap sticks. She believes that each attempt at coitus revives painful infantile memories. That the treatment by dilators used by a nurse is unsatisfactory is due also to the association of this infantile memory of trauma with women.

AN ALPHABET OF BREAST FEEDING

The author calculates that $5\frac{1}{2}$ million gallons of human breast milk were wasted in 1941 through unnecessary weaning of babies. He considers that in view of the shortage of cows' milk this merits serious consideration.

The difficulties of breast feeding are divided into

maternal and infantile with further subdivisions into general lactation suckling and digestion.

A large number of babies are weaned because the psychological state of the mother is detrimental to good lactation. Reassurance of the mother would reduce the number in this group. In general physical illness the effect of lactation on the general health of the mother should be the deciding factor.

Disturbances in lactation such as excessive enlargement of breasts or cracked nipples can be treated without the necessity of weaning. Suckling difficulties may be due to inexperience of the mother or inaptitude of the baby, and can be treated by explanation and training.

There are many difficulties with the babies digestion but with the exception of the rare anaphylactic vomiting, weaning should never be undertaken on account of vomiting. In some of the intestinal upsets such as gastro-enteritis, of the infant temporary withdrawal of milk may have to be undertaken but can be re-established when the baby commences to improve.

The author concludes by pointing out that we must understand the processes that underlie lactation, suckling and digestion in order to deal with any derangements of this normal physiological process. Human milk is the perfect food for the infant and in the arrangement for its supply and consumption is almost free from infection.

T N A JEFFCOATE

The Canadian Medical Association Journal

Vol XLVI January 1942 No 1

*Two cases of primary carcinoma of the Fallopian tube J O Baker and A Blais

Vol XLVI February 1942 No 2

*Induction of labour induction methods and dangers W S Holmes

TWO CASES OF PRIMARY CARCINOMA OF THE FALLOPIAN TUBE

Primary carcinoma of the Fallopian tubes is an extremely rare disease only 363 cases having been reported in a review by Barron in 1940. The authors wish to add two more cases to this list.

The first case was a woman 40 years of age, admitted to hospital for pain of 3 days duration

in the right iliac region. A previous attack of brief duration had occurred some months earlier. On examination marked tenderness was found over the whole abdomen, but was especially noted on the right side. General examination revealed nothing abnormal except a blood cell count of 13,200, temperature 100 degrees and a pulse rate of 90. After 3 days observation and treatment in the Fowler's position there was no remission of symptoms and the temperature increased to 101 degrees. Operation was then performed, and both Fallopian tubes and ovaries were removed, the peritoneum being drained. The patient made a good recovery and at the time of reporting was still alive.

The findings at the time of the operation were a large tumour of the left Fallopian tube, which had ruptured, the lower abdomen was filled with blood clots, the right tube and ovary were adherent in the pouch of Douglas. The pathological report was as follows: the middle third of the left Fallopian tube merged distally into a large encapsulated tumour 12 by 8 cm, a large portion of the surface of the tumour mass had broken down exhibiting a lacerated appearance. The cut surface of the tumour had a fleshy, nodular appearance, with areas which showed a yellowish fatty appearance. At the point where the tube merged into the tumour mass, a caseous whitish nodule, 2 cm in diameter was noted. The right tube showed numerous caseous nodules of tuberculosis some of them exhibiting calcification. Microscopically the tumour mass was composed of masses of epithelial cells in papillary and alveolar arrangement. The mucosa of the tube showed signs of proliferation. The diagnosis was primary carcinoma of the Fallopian tube superimposed on an old tuberculous salpingitis.

The operation was conducted in January 1927 and at the time of reporting January 1942 the patient was in good health.

The second patient was a woman of 47, previously healthy who came because of swelling of the abdomen with discomfort in the hypogastrium. The swelling began 6 months previously, when she was seen for a large umbilical hernia. Three months later an operation was performed for the cure of this hernia. At this time she was told that she had carcinoma of the abdomen. The abdomen continued to enlarge after the operation. Menstruation continued normally. General examination of the patient revealed nothing unusual. The abdomen was considerably distended with dullness in both flanks shifting on changing position. Bimanual examination was impossible to effect satisfactorily. A liver function test with bromosulphaleine was made and found to be negative. The measurement round the waist was 45 inches. She was given 0.5 cc of salyrgan intravenously and this reduced her girth one inch and her weight $1\frac{1}{2}$ pounds. Repetition was without success.

Paracentesis was performed with removal of 240 ounces of thin light brown fluid. Cultures made from the growth were negative. The specific

gravity was 1.018. There was no bile. The abdomen gradually increased in size after the paracentesis. At the time of operation free bloody fluid was removed and a mass was found involving the left Fallopian tube, which was markedly enlarged, the fimbriated end, which resembled placental tissue was attached to the parietal peritoneum. The tube and a small portion of the peritoneum were removed. Both ovaries, the right tube and other viscera in the abdomen were normal. The abdomen was drained. Recovery was fairly uneventful, with the exception of much fluid escaping through the drainage tubes for the first few days. After the tenth day she was given deep X-ray therapy. The pathological report on the right tube and peritoneum removed was adenocarcinoma of the Fallopian tube grade 3. After consultation a second operation was performed two months later. Some free fluid was present in the abdominal cavity. Total hysterectomy was performed with removal of tubes and ovaries. Recovery was uneventful.

Pathological investigation showed no sign of malignant infiltration. Her first operation was performed in 1936 and in February 1941 she was in excellent health and performing heavy manual labour.

A short bibliography is appended.

INDUCTION OF LABOUR. INDUCTION, METHODS AND DANGER

Historical records show that labour was induced by rupture of the membranes as early as 1690 but was not generally advocated until 1756. This followed a conference of physicians in London held for the purpose of devising means for avoiding Caesarean section, which was then attended by a fearful mortality. The chief indication was contracted pelvis and the indications were further extended to include almost all the complications of the last trimester. The employment of this procedure reached its peak in the first decade of the twentieth century. At this time, according to Caldwell 57 per cent of all cases at the Sloan Hospital for women had labour induced by means of bags and Voorhees is said to have used them in 25 per cent of all his cases. This led to very extensive use of this means of induction with the result that through the efforts of the unskilled in inserting the bags and dealing with subsequent

complications, its use fell into disfavour and Caesarean section returned

The mortality following Caesarean section had meanwhile decreased, chiefly as the result of two improvements. One of these was the performance of the operation before the onset of labour, the other was the employment of the extra-peritoneal route

Induction of labour means the interruption of pregnancy after the child is viable, i.e., after the thirtieth week, before which time there is little chance of its survival

The indications may be discussed briefly under each separate heading. There are three main groups: disproportion, disorders primarily affecting the mother, and disorders primarily affecting the child

Disproportion Contraction of the pelvis when this is marked induction by any mechanical means is dangerous. Caesarean section is to be performed. Here, in moderate degrees of contraction, a trial of labour, following medical induction may be made and Caesarean section performed if the natural passage is impossible. All attempts at mechanical induction must be avoided if Caesarean section is contemplated

Postmaturity and over-sized baby Each case must be judged on its own merits, but this is a condition in which induction is most frequently employed, here, too, the use of oxytocics has an important place. Rupture of the membranes is one of the best methods if the head has passed the upper strait

Diseases primarily affecting the mother *Toxaemia of pregnancy* Here induction has an important place and has done much in recent years to reduce mortality. When treatment of toxaemia fails, induction is indicated and even in fulminating toxaemia is better treatment than abdominal operations. Usually simple rupture of the membranes will suffice. Often labour is more rapid than in normal cases. Sometimes the number and violence of convulsions when present are reduced by rupture of the membranes. Medical induction by the use of quinine and pituitrin is not without danger. Pituitrin is especially liable to increase blood-pressure in toxaemic patients

Renal insufficiency These patients can be treated on almost similar lines to those suffering from toxaemia

Cardiac insufficiency In pronounced cases operative measures are highly dangerous. The bag method of induction helps in dilating the cervix. The membranes may be ruptured and delivery hastened and assisted mechanically

Essential hypertension is progressive and incurable. The risks are cerebral haemorrhage and cardiac failure, and induction of labour may prevent either of these contingencies

Tuberculosis The advice of the expert is invaluable. The chief difficulties arise in the first half of gestation. Usually it is inadvisable to interfere with pregnancy, except to hasten what is often a protracted labour in this group of patients

Diseases of blood and blood-forming organs the anaemias These seldom call for interference. A transfusion should be given before induction is undertaken

Leukaemias Leukemic patients, like the anaemic, seldom become pregnant, but pregnancy seems to have an adverse effect upon these conditions. Induction may be necessary when the condition is increasing rapidly

Diseases of internally secreting glands *Hypothyroidism* is easily treated medically. Hypothyroidism may be a serious complication, though rare. Rest and iodine treatment will suffice in most cases but partial thyroidectomy may be required when these measures fail. Induction of labour is only necessary if the heart is affected

Diabetes mellitus This is an important complication of pregnancy demanding routine care. The babies in these cases tend to be overweight and induction of labour has a place in such cases

Conditions primarily affecting the baby *Placenta praevia* A great advance in the treatment of this complication was made when Snow and Powell in 1924, demonstrated methods for localizing the placenta by radiography. Caesarean section has an important place in the treatment of these cases and artificial rupture of the membranes has its chief use in cases of marginal implantation of the placenta. The use of Willett's forceps in partial placenta praevia is also a most useful method. Central placenta praevia should always be treated by Caesarean section. Eastman, after an extensive survey of the subject, makes the following statements: blood transfusion is a prerequisite to the successful management of these cases, rectal examination is valueless and dangerous, sterile

vaginal examination should be made only after the operating room has been prepared for immediate action in uninfected cases, central and lateral placenta praevia in primigravidae are best treated by Caesarean section, most cases of marginal placenta praevia in multiparae are best treated by rupture of the membranes assisted by Willett's forceps

Premature separation of the normally implanted placenta Irving in 1938, made an extensive review of the subject and his conclusions are far reaching. Conservative measures have a much lower mortality rate than Caesarean section. These measures have as their object the control of haemorrhage and promotion of uterine contractions, thereby hastening delivery. An excellent method is to rupture the membranes tightly pack the vagina, attach a firm perineal bandage to an abdominal binder and give small repeated doses of pituitrin.

Hydramnion Usually rupture of the membranes is sufficient, as it relieves over-distension. If the presenting part does not fit well into the lower uterine segment, or if there is prolapse of the cord following rupture of the membranes a bag may be used.

Habitual death of the foetus When there is a history of habitual death of the foetus, induction of labour well in advance may frequently save the baby. Approaching death of the foetus is often foretold by a decrease in the mother's weight due to cessation of growth of the uterus. The employment of a bag is very useful.

Malposition including breech presentation When this cannot be rectified induction prematurely will often facilitate delivery. Again a bag is preferable.

Methods of delivery medical Castor oil, quinine and pituitrin are the drugs most commonly used. Small doses of quinine are often as efficacious and more so than larger doses. Pituitrin is dangerous and must be employed in small doses given repeatedly under close observa-

tion. All work with greater efficacy if the membranes are ruptured and especially if the cervix is gently stretched. Of course, the nearer the patient is to term, the better.

Rupture of the membranes This is one of the oldest and safest of methods. Occasionally, however, labour is long delayed with increasing risk of infection. In a very few cases the cord may prolapse. The effectiveness of the method is greatly increased by stretching the cervix, the administration of oxytocics and the use of a bag. It is of most value when the uterus is irritable, as in pre-eclamptic toxæmia.

Gutmacher and Douglas compared results following the use of bag, bougie and rupture of the membranes. The latter method was found more successful, with lower foetal and maternal mortality and morbidity.

Bougie The advantage of the bougie is the ease with which it can be inserted, dilatation of the cervix being unnecessary, but there are real dangers from infection following its use. Failures amount to 15 per cent to 20 per cent of all cases in which it is employed. It may be used in conjunction with medical induction and packing of the cervix and vagina.

Bags These have a threefold action, in that they mechanically dilate the cervix, stimulate uterine contractions and exert pressure upon a low implanted placenta thereby reducing haemorrhage, and when this is required bags will be found most useful. Voorhees, after 14 years' experience with bags advised their use only in cases in which the cervix was soft and easily dilated.

It is believed that 20 per cent of all deaths occurring in pregnancy follow Caesarean section, and of these 50 per cent are due to infection. Induction, therefore, has a definite place. Each case must be individually considered, and skill and judgment are often tested to the utmost in handling the emergencies which sometimes follow its use.

A short bibliography is appended.

J. LYLE CAMERON

REPORTS OF SOCIETIES

ROYAL ACADEMY OF MEDICINE IN IRELAND

A Meeting of the Section of Obstetrics of the Royal Academy of Medicine in Ireland was held in the Royal College of Physicians on Friday October 23rd, 1942. The President, Dr NINIAN FALKNER, was in the Chair.

The President, Dr FALKNER reported

TWELVE CASES OF RUPTURE OF THE UTERUS WHICH HAD OCCURRED IN THE ROTUNDA HOSPITAL IN THE PAST TWO YEARS

Of the 12 mothers, 3 died and 9 recovered. Of the 12 infants 3 recovered and 9 were lost.

Two of the children which survived were in cases in which the rupture was incomplete and the third was in a case in which the rupture of the uterus was produced during the extraction of a breech.

The first maternal fatality was undiagnosed and treated as postpartum haemorrhage. The second was undiagnosed and treated as antepartum haemorrhage, and the third was a most unusual case which followed a fall in the street. Of the mothers who recovered 4 were treated by subtotal hysterectomy and 4 by suture of the uterus. One was treated conservatively. Of the mothers who died 2 were not treated and one was treated by subtotal hysterectomy following Caesarean section.

Average age 35, average parity 5, no primigravida.

In 9 cases the patient was in labour, in 3 not in labour.

The rupture was spontaneous in 9 and traumatic in 3 cases (fall, injudicious use of forceps, and difficulty with extended arm).

The rupture was complete in 8 cases and incomplete in 4. The rupture occurred in 3 cases in which classical Caesarean section had been performed.

The diagnosis was made in 9 cases before treatment was instituted and in 7 of these it was made by co-relating the symptoms and physical signs and in 2 by directly palpating the rupture.

Dr R. M. CORBET congratulated Dr Falkner on his results and sympathised with him in having met 12 such cases in 2 years.

Dr Falkner had suggested that the treatment in Case 7 might be open to criticism. Dr Corbet thought that the treatment was entirely correct and that it was lucky that the peritoneal cavity was not entered during the manual removal. Dr Corbet said he had seen 35 cases of rupture of the uterus, 16 of which had occurred during the time he was Master of the Coombe Hospital. The mortality of the total collected series was 28.6 per cent.

About 1930 he had come to the conclusion that, if rupture were diagnosed or strongly suspected before the foetus was delivered, laparotomy should be performed, the uterus being removed or retained, according to the conditions found.

Since that time he had had 16 cases of rupture of the uterus under his care. The treatment was primary Caesarean hysterectomy in 11 cases, with one death from mesenteric thrombosis.

Laparotomy with suture of the rent was done in 2 cases, with no death and one patient died just as he arrived on the scene, before any treatment could be undertaken. From these 16 cases 8 live babies were obtained. He felt that the advice, given in so many textbooks to deliver the patient vaginally after rupture had been diagnosed, was exceedingly dangerous.

He congratulated Dr Falkner on the success which followed his conservative treatment of suture of the rent in 4 cases and felt that he himself, perhaps, erred on the side of being too radical.

Professor A. H. DAVIDSON said that it was unfortunate for Dr Falkner to have had 12 cases of rupture in 3 years. The fact that 3 of these ruptures had occurred in classical scars should he thought teach them not to do classical Caesarean sections. All ordinary sections done either before or during labour should be done in the lower

segment. He had had 16 cases of rupture with 6 deaths, which was not as good a record as either the President's or Dr Corbett's. Four of these deaths had been in patients who had been sent into the Rotunda Hospital after failed forceps. He was convinced that all cases of definite rupture in which the rupture was in the body of the uterus should be treated by laparotomy, followed by whatever treatment the doctor in charge of the case thought best. He thought that there was still a place left for conservative treatment by plugging the rent. The classical scar in a case in which the Caesarean section had been done for toxæmia was a very bad one.

Dr O'DONEL BROWNE said that the number of cases of rupture which Dr Falkner had had for the period of time was large. The chief site of rupture appeared to be the fundus. From this communication it stood out very clearly that a scar in the lower segment was very much safer than one in the upper segment.

Professor MUNRO KERR was rather inclined to favour total rather than subtotal hysterectomy. He asked if in any of Dr Falkner's cases the cervix had been split as well as the upper segment. The only case of ruptured uterus which he had had under his care was one in which he had previously done a classical Caesarean section. In this case the patient made a good recovery and the baby lived.

Dr J. G. GALLAGHER referred to ruptures of scars of previous classical Caesarean sections and asked what the position of the placenta in these cases was. How many of the cases of external bleeding had had any marked symptoms? In the case of transverse lie how long had the patient been in labour before the rupture occurred? In one case in which the uterus had been plugged, why had the tear not been discovered during the plugging? It was very extraordinary that amongst all these cases not one patient should have been a primipara. Plugging for incomplete tears seemed to have gone out of fashion altogether.

Dr JAMES APTHORP said that a very dangerous type of case was the patient who had had some form of section previously. He had always been surprised that the condition known as fibrosis uteri had never been mentioned in connexion with rupture of the uterus. He had never seen a uterus rupture after myomectomy, but Professor de Lee had mentioned it as having occurred in his practice.

Dr T. M. HEALY said that very few cases came to the operating table in as good condition as those in which classical Caesarean section had been done 20 years previously. He asked if there was a history of any internal injury in any of Dr Falkner's cases.

Dr EDWARD SOLOMONS asked if Dr Falkner had any views regarding rupture of the uterus following myomectomy.

Dr FALKNER in reply said that a desperate condition in failed forceps was when the uterus had been even partially ruptured. These cases were often in primigravidae, and when the abdomen was opened hysterectomy was the only course to adopt. This was a desperate course to have to take in such cases. It was very difficult to have to decide whether plugging the rent was going to be effective or not. There were some cases in which the control of haemorrhage could be effected only by total hysterectomy. The case of transverse lie had been treated by external version. In these cases the first thing to be thought of was the patient's life and the second thing was the necessity for preserving the function of reproduction.

Dr R. M. CORBETT read

A NOTE ON LOCAL ANAESTHESIA IN OBSTETRICS AND GYNAECOLOGY

The PRESIDENT said that this was a very apt time to bring up the question of local anaesthesia because he thought that before very long they would be in a position in Eire of having to limit the number of general anaesthetics, owing to their shortage. Dr Corbett's communication should encourage them all to make wider use of local anaesthesia in future.

Dr T. M. HEALY said that in the use of local anaesthesia the preliminary anaesthetic which was employed was half the battle. In his opinion not half enough attention was paid in the general hospitals to the anaesthetist and to the anaesthetic. Patients who were badly anaesthetized vomited, coughed and hurt their stitches. Very junior people should not be allowed to give anaesthetics to patients who were likely to have a long convalescence. Dr Corbett's method of anaesthesia was peculiarly suitable to private patients or to a maternity hospital. It was not so applicable to patients in a general hospital. The use of local

anaesthesia taught the operator accuracy and gentleness, two most important things

Professor A H DAVIDSON said that anaesthesia was as much of a specialty as obstetrics, or any of the other branches of medicine, and yet no effort had been made to treat it as such. The time had now come when every hospital should have an assistant anaesthetist. He had learned the technique of local anaesthesia in Vienna and had learned to give novocaine and adrenaline alone. Since then vaginal work had become to him a great pleasure rather than a severe trial. Referring to caudal anaesthesia, he said that the only disadvantage about it was that one had to wait for 15 minutes before putting novocaine into the vaginal canal. Caudal anaesthesia however, was very quick, very simple, and very safe. He had performed over 200 vaginal hysterectomies under local anaesthesia, and could not remember one case in which he could blame the local anaesthetic for secondary haemorrhage.

Dr O FITZGERALD said he had always been surprised at how little use was made of local anaesthesia in gynaecology. When in Philadelphia four years ago he had seen caudal anaesthesia used and since then he had used it to a considerable extent. After the introduction of the needle it was necessary to be very sure that one had not perforated a possibly low lying sac into the intradural space. He asked if Dr Corbet had had any trouble with his patients suffering from severe nausea at any stage. Sometimes it occurred in the middle of the operation and was extremely disconcerting both to the anaesthetist and to the operator.

Dr R W SHAW said that spinal anaesthesia did not always work, and intravenous anaesthetics were not always quite safe. Dr Corbet's method of anaesthesia was an excellent one, and there was undoubtedly a very large place in surgery for local anaesthesia. One of the reasons why local anaesthesia had not been more extensively tried was because there was an idea that it took longer than general anaesthesia. He asked Dr Corbet why he preferred to give morphia and scopolamine subcutaneously rather than the barbituric drugs by the mouth. In his opinion the likelihood of post-operative respiratory trouble was increased by the use of morphia. The question of doing major operations under local anaesthesia was a difficult

one. Nearly all Dr Corbet's cases had been hospital patients. He thought the average private patient preferred to be put asleep. He did not think that there was much likelihood of a shortage of anaesthetics because both nitrous oxide and chloroform were manufactured in Eire. Caudal anaesthesia was a very useful method indeed, but it was not altogether as simple to administer as Dr Davidson had suggested. It was sometimes not so easy to get the needle into the sacral hiatus.

Dr Corbet thanked the President and the Section for the kind way in which they had received his paper.

He said he thought the method ought to be extended in Caesarean section but that he was often impatient of the time spent in using the local anaesthetic. He thought the premedication was of very great importance, and that the barbiturates were excellent when the patient was going to have inhalation anaesthesia, but, from his experience of them during labour, he considered morphia and hyoscine preferable when the patient was going to have pain or discomfort.

He had not used caudal anaesthesia, and was interested in Professor Davidson's, Mr Fitzgerald's and Dr Shaw's remarks on the subject but one of his colleagues had once accidentally entered the subdural space and produced paralysis, almost to the clavicles.

He did not know whether novocaine produced nausea or not because he had always ascribed any vomiting which followed this method to the morphia. He thought there was a definite danger when injecting the novocaine into the veins of the parametric tissue if the precautions prescribed were not taken. He had sucked back blood into the syringe on at least three occasions.

He used the method in private practice and so far, the patients on whom he had operated had been very pleased with it.

He endorsed the views of Dr T M Healy, Professor Davidson and Dr R W Shaw on the importance of the anaesthetist, and he would be delighted to have a full-time experienced anaesthetist at his service, but, regrettably, that was not so.

The saving of ether ran into the neighbourhood of 100 bottles per annum.

He again thanked the Section for the way in which they had received his communication.

THE Journal of Obstetrics & Gynaecology of the British Empire

VOL 50, No 3

NEW SERIES

JUNE, 1943

Unsuspected Tuberculosis of the Endometrium

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A STUDY of the literature on tuberculosis of the endometrium shows that 3 varieties of this condition exist. The first type, which is quite common, forms part of a widespread genital tuberculosis which chiefly affects other pelvic structures, particularly the Fallopian tubes. In the second type, which is rare, the tuberculous infection is very gross but is confined to the body of the uterus. The endometrium in this variety is replaced by a layer of tuberculous granulation tissue and little trace of the original structure can be found on histological examination. The third type, which is generally thought to be still rarer, is also limited to the uterine body. On microscopic examination the tuberculous lesions are isolated and infrequent, and the remainder of the endometrium appears to be normal. This third type forms the essential subject of the present paper.

The first recorded case of tuberculosis of the uterus was described by Morgagni.¹ Since then many papers have been published dealing partly or wholly with tuberculosis of the uterus, and among the most notable of these may be mentioned contributions by Comyns Berkeley,² Daniel,³ Greenberg,⁴ Jameson, Murphy,⁵ Norris⁶

and Williams.⁷ An extensive review of the literature is given by each of these authors.

INCIDENCE OF TUBERCULOSIS OF THE ENDOMETRIUM

The findings of the present investigation show that the third type of endometrial tuberculosis is relatively common, and that in these cases the principal complaint is usually one of sterility. These conclusions are arrived at as a result of an analysis which was made of the histological preparations of the Pathological Department of the Royal Samaritan Hospital for Women from January 1, 1935, to December 31, 1941. During this period 5,521 curettings and 864 uterine specimens were examined histologically. In the curettings, tuberculosis of the endometrium was found in 61 specimens (1.1 per cent). In the uterine specimens tuberculosis of the endometrium was found in 12 cases (1.4 per cent). The 73 specimens were obtained from 58 cases.

LITERATURE ON THE INCIDENCE OF TUBERCULOSIS OF THE UTERUS

In the following papers the number of curettings showing tuberculosis on histolo-

gical examination and the total number of curettings examined is given Dogra¹⁰ 10 in 1,052 (1 per cent), Martin¹¹ 22 in 1,500 (1.5 per cent), Rock and Bartlett¹² 8 in 457 (1.7 per cent, this material was obtained by endometrial biopsy from 329 patients) These figures are in fairly close agreement with the present findings of 61 in 5,521 (1.1 per cent) On the other hand, Domínguez¹³ only found tuberculosis 5 times in 5,156 endometrial specimens examined histologically (0.1 per cent)

A number of other authors give the percentage of all cases of genital tuberculosis in which uterine involvement was found Bertolini¹⁴ (12.7 per cent), Caffier¹⁵ (50-70 per cent), Cummins¹⁶ (50 per cent), Daniel¹ (10 per cent), Dickinson¹⁸ (40 per cent), Diethelm and Ramsey¹⁹ (3 per cent), Fehling²⁰ (50 per cent), Fuhrmann²¹ (50 per cent), Goodall²² (12 per cent), Horizontow²³ (47.8 per cent), King²⁴ (50 per cent), Kroemer²⁵ (25.1 per cent), Labhardt²⁶ (13.7 per cent), McArdle²⁷ (75 per cent), Merletti²⁸ (43.6 per cent), Mosler²⁹ (66-76 per cent), Neu³⁰ (14.6 per cent), Norris³¹ (50 per cent), Peterson³² (50 per cent), Polano³³ (50 per cent), Schramm³⁴ (20.6 per cent), Simmonds³⁵ (76 per cent), Smith³⁶ (22 per cent), Spaeth³⁷ (66-76 per cent) So far as can be judged, these authors do not refer in any way to the present variety of case, in which tuberculous endometritis is found without any other evidence of genital tuberculosis Many other authors have discussed the incidence of uterine tuberculosis, the estimates of frequency varying from "common" to "extremely rare", since figures are not given and as the precise type of lesion to which they refer is frequently not stated, this group of references will not be quoted separately

PRESENT SERIES

Out of the gross total of 58 patients with all types of tuberculous endometritis, 24 are

excluded from consideration in this paper as they are of type 1, i.e. they showed evidence, clinical or pathological, of involvement of other pelvic organs in the tuberculous process The remaining 34 patients with 49 examinations of endometrium form the subject of the present study One of them shows the second type of endometrial tuberculosis, the aspects in which this case differs from the others will be discussed in the appropriate sections of the paper The other 33 are of the third type, with scanty miliary tubercles in otherwise normal endometrium The only comparable series which could be found in the literature was the report of 12 cases of tuberculosis apparently confined to the endometrium which was recently published by Schockaert and Fern³⁸ The total number of specimens in which these cases were found is not stated

Diagnosis

In all cases in the present series there was nothing to suggest before operation that uterine tuberculosis was present The difficulty of diagnosis of uterine tuberculosis on clinical grounds alone has been stressed by a number of writers, some of whom state that symptoms may be completely absent Daniel,¹ Deelman,³⁹ Diethelm and Ramsey,¹⁹ Gerich,⁴⁰ Goodall,²² Gupta,⁴¹ Hussy and Vetter,⁴² Jameson,⁴ Kelly,⁴³ Keogh,⁴⁴ Lapeyre and Guibert,⁴ Lenormant,⁴⁵ v Paulsen,⁴⁶ Thomson,⁴⁷ Weiss⁴⁸ Every case in the series described by Schockaert and Fern³⁸ was undiagnosed before operation In the present cases diagnosis was made in every instance by histological examination of the endometrium, supplemented in many instances by bacteriological investigations

CLINICAL ASPECTS

The present series can be divided into two main groups The larger group consists of

24 patients in whom the principal and frequently the only complaint was sterility. The patient with advanced uterine tuberculosis is in this group. In the smaller group of 10 cases the principal complaint in 9 instances was profuse and sometimes irregular menstruation, the main complaint in the remaining patient was vaginal discharge. Separate analysis of these groups did not reveal any significant difference apart from age distribution, it is thus desirable to consider them together throughout the paper. In Schockaert and Fern's³⁸ cases the primary complaint in 8 instances was sterility and in the remaining 4 was profuse and sometimes irregular menstruation.

Pelvic Aspects

Menstrual history The patient with gross tuberculosis of the uterus had primary amenorrhoea. Eight other patients had profuse and irregular uterine bleeding. The menstrual cycle in the other 25 patients showed only minor deviations from normal. The onset of puberty was within normal limits in every case. Thirteen patients had dysmenorrhoea, 4 had profuse menstruation, 4 had irregular menstruation and 1 had scanty menstrual periods. Four of Schockaert and Fern's³⁸ patients complained of uterine bleeding, 2 had scanty menstrual periods and 1 had dysmenorrhoea.

Previous pregnancies Thirty-two of the 34 patients were married. The average number of years married was 8, the shortest period being 1 year and the longest 47 years. Only 5 of the 34 patients had had any previous pregnancy. One patient gave a history of a miscarriage only. The remaining 4 patients had had 1, 2, 4 and 9 full-time pregnancies respectively, one of these patients had also had a miscarriage. This high incidence of sterility in endometrial tuberculosis is striking. It is not possible to give the exact number of sterility pa-

tients from which these cases are derived. Sharman⁵⁰ found tuberculosis of the endometrium in 20 cases out of a total of 390 patients complaining of sterility, in whom the endometrium was examined histologically (5.1 per cent). Nineteen of these cases are included in the present series, the remaining patient was excluded because slight tubal thickening was found on clinical examination. Steinsick⁵¹ found 7.2 per cent tuberculosis of the endometrium in 212 patients complaining of sterility, and Schockaert and Fern³⁸ 7 per cent tuberculosis of the endometrium in 71 sterility cases.

The importance of endometrial tubercle as a causal factor in sterility has been stressed by a number of writers. Bulman,⁵² Courriades and Jaulain,⁵³ Daniel,⁵⁴ Eden and Lockyer,⁵⁴ Halban and Seitz,⁵⁵ Hoppner,⁵⁶ Kraul,⁵⁷ Muret,⁵⁸ Rock and Bartlett⁵² Tamus,⁵⁹ Vogt,⁶⁰ Williams.⁹ On the other hand, Jameson⁷ is of the opinion that sterility as a symptom of uterine tuberculosis has been overemphasized. In his cases of uterine tuberculosis (mostly examples of gross genital tubercle) parous patients outnumbered nulliparous patients by 2 to 1. The higher incidence of uterine tuberculosis in parous patients has also been stressed by Murphy⁷ and by Greenberg⁴ (58.6 per cent of parous women compared with 39.6 per cent of nulliparous women had uterine tuberculosis in his series of 200 cases of tuberculous salpingitis). When these findings are compared with the present series, it is seen that while gross genital tuberculosis may show a higher percentage of uterine involvement in parous than in nulliparous patients, tuberculosis apparently confined to the endometrium is much commoner in patients who have not been pregnant.

It is fairly easy to understand why this high incidence of endometrial tuberculosis in cases of sterility has not been more generally recognized.

(a) Routine histological examination of the endometrium was frequently omitted in the past, in recent years this has been carried out with greater frequency in order to obtain evidence of ovulation

(b) The lesions of this third type of endometrial tuberculosis are easily overlooked as they are small and scanty. With increasing experience one's visual acuity for the lesions becomes correspondingly increased, but as will be shown later they are found in many cases only after diligent search

(c) Even when the lesions are seen, their tuberculous nature is often not obvious to the observer with an inadequate background of general pathology

(d) It is possible that the increasing incidence of tuberculosis in general may also apply to tuberculosis of the endometrium

Other symptoms Vaginal discharge was complained of in 18 cases. The only other symptoms which were relatively frequent were lower abdominal pain unconnected with menstruation (5 cases), increased frequency of micturition (5 cases), and dyspareunia (5 cases)

Pelvic examination The following lesions were found on pelvic examination

Mobile retroflexion of uterus	6 times
Slightly enlarged uterus	3 times
Slight cystic enlargement of one ovary	3 times
Prolapse of vaginal walls	Once
Cervical erosion	Once
Uterine fibroids	Once

These conditions were found in 13 of the 34 cases in the series, in the remaining 21 patients pelvic abnormality of any type was not found. The following lesions were found in Schockaert and Fern's³⁸ cases on pelvic examination

Cervicitis	4 times
Enlarged uterus	Twice
Uterine fibroids	Twice
Cervical stenosis	Once
Uterine hypoplasia	Once
Enlarged and tender adnexa	Once

Parametritis	Once
Fixed retroversion	Once
Perimetrial adhesions fixing uterus	Once

The above lesions were found in 11 of the 12 cases in Schockaert and Fern's³⁸ series, the remaining patient did not show any pelvic abnormality. Although the writers say that they have excluded all cases in which the clinical examination suggested probable genital tuberculosis, in 4 of their cases there is at least a suspicion that the tuberculous process is not confined to the endometrium. The lesions in these cases are the last four in the list. In the present paper all patients with any lesions of these types were excluded

Surgical Investigation and Treatment

Dilatation of the cervix and curettage of the uterus were performed in 24 cases. In 9 other instances full curettage was not carried out and the diagnosis of tuberculosis of the endometrium was made from material removed by endometrial biopsy at the sterility clinic. In the remaining patient, in whom uterine fibroids had been found, subtotal hysterectomy was performed for this condition, the Fallopian tubes and ovaries appeared to be healthy and were conserved

Tubal patency Tubal insufflation was carried out in 20 of the 24 sterility patients. The Fallopian tubes were found to be patent in 4 cases and blocked in the remaining 16. In one of the patients, in whom the Fallopian tubes were patent, the insufflation was repeated 18 months later and the Fallopian tubes were found to be blocked. Palpable thickening of the Fallopian tubes was not present in any case. Bulman,³² Hoppner⁶ and Tamis³⁹ each report a case of apparently uncomplicated endometrial tuberculosis in which tubal insufflation showed the Fallopian tubes to be patent. Schockaert

and Fern¹⁸ found tubal patency in 5 of their 8 sterility patients in whom tubal insufflation was carried out

The percentage of cases in the present series with blocked Fallopian tubes (80 per cent) is much higher than that found in general sterility cases. In 480 cases of sterility in which tubal insufflation was performed, Sharman²⁰ found that only 38 per cent showed tubal occlusion. It is possible that the higher incidence of tubal blockage in the patients with tuberculosis of the endometrium may be due to a sub-clinical involvement of the Fallopian tubes by tuberculosis, but this hypothesis has not been tested by pathological examination of the Fallopian tubes in any of the present cases. Siddall⁶¹ reports a case of tuberculosis of the endometrium accidentally discovered by curettage, when hysterectomy and bilateral salpingectomy were performed, the tuberculous lesion was found to be limited to the endometrium. Novak⁶² is of the opinion, however, that when curettage reveals tuberculous endometritis, one is justified in assuming that tuberculous disease of the Fallopian tubes is also present, even though clinical evidence of the latter cannot be found. In all his cases of this type in which laparotomy was later performed, unquestionable evidence of tubal tuberculosis was discovered.

In 4 of the cases in which tubal insufflation had demonstrated tubal blockage, injection of Lipiodol was employed. In each case the blockage was confirmed by X-ray examination. It is of interest to note that calcified abdominal glands were not seen in any of these films.

Presence of ovulation Endometrium was removed premenstrually in 16 cases in the present series. The endometrium had the normal appearances of the secretory phase of the menstrual cycle in 11 of these. In the other 5 cases evidence of secretory activity was absent in one or more speci-

mens, the subsequent menstrual period followed within a day or two after the biopsy in each instance. Such histological appearances can be taken as presumptive evidence of absence of ovulation. The incidence of a periodic or total anovulatory cycle in the present series (nearly one third of the cases) is very high when compared with a general series of sterility cases. Sharman²⁰ found that only 18 (1 e 5 2 per cent) of 342 sterility cases unassociated with tuberculosis, when the endometrium was examined premenstrually, had a periodic or total anovulatory cycle. The present figures are too small to be significant, and further study of this aspect is obviously required.

General Clinical Aspects

Age incidence The age of the patients complaining of sterility ranged from 21 to 30 years (average 26 years). The age of the remaining patients ranged from 18 to 66 years (average 39 years). The age incidence of Schockaert and Fern's¹⁸ cases was in reasonable agreement with the present series.

Previous health Investigation of the previous health revealed the following conditions indicating or suggesting previous tuberculous infection: pleurisy 3 cases (1 with effusion), tuberculosis of abdominal glands 2 cases (1 in childhood), tuberculosis of neck glands 1 case. Four of Schockaert and Fern's¹⁸ patients had previous illnesses which might have been tuberculous in nature. 3 patients had pleurisy in adolescence and one had caries of the bones of the right foot in childhood.

General examination Mild anaemia was found in 1 case. In a second a subsiding bronchitis was present, and in a third case there were physical signs of active pulmonary tuberculosis which was confirmed by X-ray examination. The remaining patients were healthy in appearance and

without any abnormality on systemic examination. Ten of Schockaert and Fern's²⁸ patients appeared to be in excellent health, of the remaining 2, 1 had exophthalmic goitre, the other had lost a great deal of weight. Clinical examination of these patients did not show any evidence of pulmonary disease, 2 had X-ray examination of the chest, the only abnormality found in 1 being evidence of old pleurisy.

Temperature and pulse-rates An analysis was made of the temperature and pulse charts in the 27 cases in which such records were available. These charts were only the ordinary morning and evening hospital records and the observations had not been made with any unusual precautions. A study of the charts did not show any evidence of an active tuberculous lesion. One patient had intermittent elevation of pulse-rate and temperature, she was found to have a severe coliform infection of the urinary tract. Four other patients had slight post-operative elevation of pulse-rate or temperature for a day or two. In the remaining 22 patients the temperature and pulse-rate remained normal throughout.

PATHOLOGY

Naked Eye Examination

Naked eye examination of the curettings obtained did not show any abnormality. The more gross forms of endometrial tuberculosis with caseation and extensive ulceration were not seen in any specimen. In the one uterine specimen the endometrium appeared to be normal on inspection.

Histological Examination

In every case except the one with type two lesions the histological appearances were similar. The picture was one of infrequent, and usually isolated, small tubercles scattered irregularly through the endome-

trium (Fig 1). Occasionally a cluster of tubercles could be seen in a single microscopic field (Fig 2). These two photographs should be looked at from a distance of several feet. In the great majority of cases, however, the lesions were extremely scanty, and careful search through a slide of all the endometrium removed in a thorough curettage sometimes revealed only a single tuberculous focus, most of the fragments appearing absolutely normal. In most cases the tuberculous foci occurred mainly towards the surface of the endometrium, but in a few instances, particularly when they were fairly frequent, they were seen at all levels.

The individual tuberculous lesions are quite characteristic. A central zone of epithelioid cells is always present, and usually, though not invariably, one or more giant cells can be seen. A small central area of caseation is sometimes present. The focus is usually surrounded by a zone of lymphocytic infiltration. The glandular structure in the endometrium does not show any abnormality, apart from the glands in the immediate vicinity of the tuberculous foci. In many cases the stroma is infiltrated throughout with lymphocytes and plasma cells in moderate numbers, and in an occasional specimen this chronic inflammatory reaction is very marked. The histological picture is that usually described as miliary tuberculosis of the endometrium, though in most of the specimens in the present series the individual lesions were much less frequent than in the majority of the cases reported in the literature.

On measurement the average size of the tubercles was found to be 0.21 mm. This figure was obtained by measuring 100 individual lesions, one or more being included from every specimen in which such localized lesions were found. The smallest tubercle measured 0.14 mm and the largest 0.33 mm. The true average size of the tuberculous foci is probably much larger.



FIG 1
Single tubercle in endometrium



FIG 2
Group of tubercles in endometrium

than 0.21 mm as serial sections were not obtained, and it is almost certain that in many instances the section did not pass through the centre of the tubercle. Even in a single piece of endometrium the size of the tubercles was found to vary considerably, it is not possible to say whether this variation was due to a true difference in size or merely to the cutting of the lesions at different levels.

In only 1 case were the histological appearances different from those just described. This was the patient with advanced tuberculosis confined to the uterus. Several endometrial biopsies were made in this case, on each occasion the curettings were scanty and were composed entirely of tuberculous granulation tissue, no glands being present.

Relation of Tuberculous Lesions to Stage of Menstrual Cycle

The size of the tubercles appeared to be approximately the same at all stages in the menstrual cycle, in each specimen taken during the first half of the cycle one or more lesions near the maximal diameter of 0.33 mm were seen. Central caseation in the lesions was more frequently seen towards the end of the cycle. Jameson⁵ states that in most cases in which a diagnosis of tuberculosis of the endometrium was made by examination of curettings, the endometrium was in the premenstrual phase of the cycle. He is of the opinion that examination at this stage gives the best chance of success. In 58 specimens in the present series the time in the menstrual cycle at which the tissue was removed was noted, and the results are analysed in Table I. It will be seen from the table that in cases of proved endometrial tuberculosis, the chances of finding tuberculous lesions on histological examination are not significantly different at any stage of the menstrual cycle.

TABLE I

Time of removal of endometrium in relation to finding of tuberculous lesions in known cases of tuberculosis of the endometrium

Time in menstrual cycle at which endometrium was removed	Specimens showing tuberculous lesions	Specimens not showing evidence of tuberculosis
1st to 7th days	0	1
8th to 14 days	8	4
15th to 21st days	8	5
22nd day and over	22	10

Additional endometrial biopsies Additional endometrial biopsies were performed on one to four occasions in 21 of the 28 patients traced. The curette used in all the endometrial biopsies in this series was of the type designed by Sharman and Sheehan⁶. It is of interest to note that in every case the cervix appeared to be healthy. In only 10 of the 21 patients were tuberculous lesions found in every specimen examined. This shows that the tuberculous lesions of the endometrium in the present series of cases are often very scanty. A single negative biopsy in cases of sterility or functional uterine haemorrhage does not eliminate the possibility of tuberculosis of the endometrium. A thorough curettage with histological study of all the endometrium removed should be carried out in all such cases. The advisability of examining several sections of endometrium before excluding tuberculosis has been stressed by Dogra,¹⁰ Hohné¹¹ and Jameson.⁵

In 3 of the cases in which inoculation of a guinea-pig with tissue removed by endometrial biopsy gave a positive result, histological examination of endometrium removed simultaneously did not show any evidence of tuberculosis. Serial sections were then made of all the tissue remaining in the 3 blocks, and in 2 of the cases tuberculous

foci were found in this detailed search. This emphasizes the fact that reliance must not be placed on a single section in eliminating tuberculosis of the endometrium.

In known cases of tuberculous endometritis, examination of single slides gives negative findings in a third of the cases. In the present paper the incidence of tuberculosis is recorded as 11 per cent of all curettings examined, but these examinations were nearly always made on single sections. If serial sections of all curettings had been studied it may reasonably be considered that an incidence of at least 16 per cent would have been found. It is very possible that if routine guinea-pig inoculations had been made from every curetting, a higher percentage still would have been found. The same considerations apply to the incidence of tuberculous endometritis in patients with sterility, the figures of 5 to 7 per cent quoted previously are presumably an underestimate of the true incidence.

DISCUSSION

The above findings show that it is quite easy to miss tubercles in the endometrium unless plenty of tissue is examined and serial sections are studied. Nevertheless there seems to be some difficulty in recognizing tubercles in the early part of the menstrual cycle, there was not a single case identified as tuberculous endometritis among the patients curetted during the first week of the menstrual cycle.

This raises the very interesting question of whether the tubercles grow as a fresh crop in each cycle of the endometrium and are shed at menstruation, or whether they remain continuously in the endometrium. The former view is in accordance with most of the findings.

(a) The tubercles are chiefly situated in the superficial layers of the endometrium.

(b) They are always miliary in type and

have histological appearances suggesting an age of a few weeks at most.

(c) Central caseation is most marked towards the end of the cycle.

(d) Even if they are present in the first week of the cycle as histologically recognizable entities, they must be very small and widely separated, so that, in fact, they could not be identified in the present study, even though nearly all the patients at this stage were fully curetted.

The tubercles appear to be more numerous and more easily recognized in the last week or two of the cycle. The proportion of positive specimens in Table I is high in the last week despite the fact that 26 of the 32 examinations at this stage were made on only a small biopsy fragment of endometrium. On the other hand the tubercles in the second week of the cycle are of the same average size as in the last week of the cycle, it is difficult to bring this into agreement with the view that all the tubercles are shed at menstruation.

Assuming that there is a shedding of the tubercles at menstruation, the further question arises of how the continuous reinfection occurs. Jameson⁵ suggests that it may be from diseased Fallopian tubes, other possibilities are that tubercles remain in the basal layer and spread to the developing endometrium or that reinfection occurs from infected menstrual blood. Information on this matter could be obtained from two sources.

(a) Thorough curetting or hysterectomy in the first 2 or 3 days after menstruation, with detailed histological study of all the endometrium.

(b) Bilateral salpingectomy followed by frequent biopsy and inoculation of the endometrium into guinea-pigs for several months afterwards to see if a cure was obtained. It has, unfortunately, not been possible to carry out either of these procedures in the present study.

BACTERIOLOGY

Examination of Endometrium for Tubercle Bacilli

The difficulty of finding tubercle bacilli in the endometrium in tuberculous endometritis has been emphasized by the following writers: Jameson,⁵ Pozzi,^{6a} Schottlander,^{6b} Steven,^{6c} Stewart,^{6d} Tamis,⁹ Teacher,^{6e} Thomson,¹⁸ Vineberg.¹⁹ The cases referred to by most of these authors were of the gross type. An attempt was made in the present series to find tubercle bacilli in the endometrium by the Ziehl-Neelsen method of staining in 41 of the 49 specimens showing tuberculous lesions. Tubercle bacilli could not be found by this method in any of the sections examined. This is, however, not in any way to be taken as evidence against the tuberculous nature of the lesions, as is well known to anyone who has tried to find the organism in sections of tuberculous lesions in other parts of the body. Staining of the vaginal secretions for tubercle bacilli as suggested first by Babes²¹ and Cummings²² was not employed in any of the present cases.

Guinea-pig Inoculation

Injection of a guinea-pig with tissue removed by endometrial biopsy was carried out in 16 of the patients. The method employed was as follows. The material obtained by endometrial biopsy was placed in 1 to 2 c.c. normal saline and left in the incubator for an hour or two until ready for use. The tissue was then ground up and mixed with the saline, and the fluid was injected subcutaneously into the inner aspect of the thigh of the guinea-pig. The animal was killed 6 to 8 weeks later. The tuberculous lesions at 6 weeks were very early and were confined to the spleen, it is better to leave the animals for 8 weeks as the lesions are then much more extensive.

The results obtained were as follows. In 6 of the 16 guinea-pigs evidence of tuberculosis was not found. As will be discussed later, these cases may very tentatively be regarded as possibly healed. A portion of endometrium, taken at the same time as that injected into the guinea-pig, was examined in 3 of the 6 cases, evidence of tuberculosis was not found in any of these specimens.

In the other 10 animals extensive tuberculosis was present. This was confirmed in all cases by finding tubercle bacilli in smears taken from the splenic lesions. Endometrium taken at the same time as that injected into the guinea-pig was examined in 8 of the 10 cases. Tuberculous lesions were seen in 7 of the 8 specimens examined. As has already been mentioned, a study of single sections of these specimens showed tuberculous lesions in only 5 cases, the other 2 cases were proved histologically only after cutting serial sections of all the tissue available. It is thus re-emphasized that while a positive endometrial biopsy indicates that the tuberculous infection is still present, a negative biopsy does not in any way prove that the condition is healed. Negative serial sections are of more value than a negative single slide in assessing the progress of a case. There is, of course, a much greater chance of including one or more tuberculous foci in the amount of endometrium used for guinea-pig injection than in a single microscopic section.

In 7 of the cases in which inoculation of a guinea-pig was positive, inoculation of culture media was carried out from the splenic lesions. Löwenstein's medium was inoculated in every case, and in several instances Dorset's egg medium and Petrognani's medium were employed in addition. Direct culture from endometrium was not attempted. A growth of tubercle bacilli was obtained in 4 of the 7 cases. One was of the bovine type and 3 were of the human type.

AETIOLOGY

A great deal has been written in the literature on the subject of primary tuberculosis of the uterus. This term is quite unsatisfactory as it is impossible to prove that tuberculosis ever begins in the uterus. Although evidence of tuberculosis of other pelvic organs could not be found in any of the 34 cases in the present series, and although active tuberculous foci in other parts of the body were only found in a small proportion of the cases, there does not seem to be any justification for considering a case to be one of primary uterine tuberculosis on clinical grounds alone. The possibility of a subclinical tuberculous infection of the Fallopian tubes cannot be excluded, and it is also impossible to eliminate with certainty latent tuberculous lesions in other organs, particularly the lungs, lymph glands and peritoneum.

Health of Husbands

It was not found practicable in this investigation to make an examination of all the husbands for evidence of genital tuberculosis. Five of the husbands were examined in the Urological Department of the Glasgow Royal Infirmary. Evidence of genito-urinary tuberculosis was not found in any of these men, the only abnormality discovered being marked deficiency of spermatozoa in the seminal fluid in one case.

The patient was asked about her husband's health in 19 of the present cases, in 18 instances the husband was said to be healthy and in most cases was engaged in heavy manual labour. The husband of the remaining patient had died of pulmonary tuberculosis 4 years after the initial diagnosis of tuberculosis of the endometrium in the wife had been made, he had been ill for 10 years and was nursed by his wife.

The possibility of transmission of tuber-

culosis during coitus in cases in which the husband is suffering from tuberculous disease of the genital organs was first suggested by Cohnheim¹ and Verneul.² This question has since been discussed in numerous papers, and it is generally agreed that although such an occurrence is extremely rare there is a definite possibility that primary tuberculosis of the cervix or body of the uterus may develop in this manner. A number of cases of transmission of genital tuberculosis in this way have been reported. It has also been suggested that primary uterine tuberculosis may develop in instances in which the husband is suffering from pulmonary tuberculosis. Bauereisen³ has reported a case in which an autopsy was performed on the widow of a man suffering from pulmonary tuberculosis, the only evidence of tuberculous disease was a local infection of the endometrium.

FOLLOW-UP

Of the 34 patients in the present series 6 could not be traced after leaving hospital. The average duration of the follow-up in the remaining 28 cases was 3 years, the longest period being 7 years and the shortest 6 weeks.

Menstrual changes In 4 patients profuse menstrual periods had become normal and in 1 an irregular cycle had become regular. In 2 other patients an artificial menopause had been produced, 1 by deep X-ray therapy, the other by hysterectomy. Menstruation was unchanged in the remaining patients.

Pregnancy Pregnancy had not occurred in any of the patients traced. A number of authors, however, have reported cases in which pregnancy developed in a tuberculous uterus. Casper,⁴ Cooper,⁵ Cuzzi,⁶ Deymel,⁷ Kraus,⁸ Mensing,⁹ Schmorl and Kockel,¹⁰ Schull,¹¹ Thorn.¹² The subject is discussed in detail by Fruhinsholz and

Feuillade⁵⁵ Cornil,⁵⁶ Hoffmann,⁵⁷ Leuret⁵⁸ and Moulouguet⁵⁹ consider that pregnancy may aggravate the tuberculous genital lesion, while Moulouguet⁵⁹ states that the child may be affected by the tuberculous infection. Cases of pregnancy in a tuberculous Fallopian tube have been described by Hoppner,⁵⁶ Stein⁵⁰ and Stevenson and Wharton,⁹¹ and the literature on such cases is reviewed in these papers.

In view of the fact that most of the cases of uterine tuberculosis reported by these authors were of the gross type, it appears that pregnancy is not impossible in the present type of uterine tuberculosis if the Fallopian tubes are not occluded. It should be noted here that the numerous cases reported in the literature of acute generalized tuberculosis arising in the puerperium and involving the uterus are outside the scope of the present discussion.

Pelvic examination. A pelvic examination was made in 25 of the 28 patients followed up. In 23 cases the pelvic findings were exactly as before, and there was not any evidence of spread to other pelvic organs. There was gross involvement of both Fallopian tubes in one of the other cases, the pelvic spread was confirmed at laparotomy. In the remaining case a small right-sided ovarian cyst was found to have developed.

Spread of Tuberculosis to Other Organs Outside the Pelvis

In 2 patients tuberculosis of the spine had developed, one patient ultimately died from this disease, the other is having sanatorium treatment. The latter was the patient who had had uterine fibroids and had been treated for this condition by subtotal hysterectomy. A study of the literature reveals only one case of spread of tuberculosis from the uterus to the spine (Turner⁹²), but a number of authors have described cases in which uterine tuberculosis was later fol-

lowed by tuberculous meningitis. Astruc,⁹³ Braye,⁹⁴ Henkel,⁹⁵ Paviot,⁹⁶ Weil⁹⁷

The chest was X-rayed in 17 cases. The findings were quite negative in 13 of these. In 3 patients radiological signs of active pulmonary tuberculosis were found. One of these, as noted previously, had well-marked physical signs when first seen, in the other 2 patients the chest had appeared normal clinically when they were in hospital. Spread to other pelvic organs was not found in any of these patients. In the fourth case healed tuberculous lesions of both lungs were found, this is the patient who later died of spinal tuberculosis, which was discovered radiologically at the same time as the healed pulmonary lesions. Curtis⁹⁸ states that almost every case of uterine tuberculosis is associated with a pulmonary lesion, but the present investigation does not support this view. A history suggestive of tuberculosis was given in only 1 of the 4 patients with X-ray evidence of pulmonary tuberculosis, this patient had had pleurisy with effusion 7 years previously.

A number of writers are of the opinion that there is a danger of spread of the tuberculous process following minor operations by the vaginal route in patients with tuberculosis of the uterus, actual examples of this have been described by Barthélemy,⁹⁹ Bungeler,¹⁰⁰ Diethelm and Ramsey,¹⁰¹ Grafenberg,¹⁰² Monch,¹⁰³ Muret⁹⁸ and Péraire.¹⁰⁴ On the other hand, Muret⁹⁸ and Vogt¹⁰⁵ state that such danger is slight. In most of the cases cited it could not be ascertained whether the original condition was confined to the uterus or whether the adnexa were also involved. One would expect a much greater tendency to distant spread in cases of widespread pelvic tuberculosis treated surgically, but the literature on the subject does not suggest that this is the case. Evidence of local or distant spread of the tuberculous process was not found in any of the present cases during their stay in

hospital after operation. Of the 5 patients who showed spread of the tuberculous process when followed up, one had had subtotal hysterectomy performed. The other 4 patients had all had dilatation of the cervix and full curettage carried out, 2 of them also had had tubal insufflation and 3 had had one or more endometrial biopsies. It is of interest to note that in the patient with pelvic spread of the tuberculosis, tubal insufflation was not performed.

PROGNOSIS

A great deal has been written in the literature on the prognosis of genital tuberculosis in general, but the prognosis in cases of tuberculosis apparently limited to the endometrium has received little attention. Daniel³ considers that the outlook in such cases must be regarded as grave and states that death may result. Consequently he advocates hysterectomy in every case. Bush¹⁰⁴ is of the opinion that a tuberculous uterus cannot be left with impunity, but does not think that the danger of leaving it is great.

Of the present patients followed up, only one had any active treatment after the diagnosis of endometrial tuberculosis had been made, this patient was treated by deep X-ray therapy and 2 years later was free from symptoms and did not show any sign of spread of the tuberculous process.

A study of the present series shows that the prognosis in tuberculosis apparently confined to the endometrium must be guarded. Of the 28 patients traced, tuberculosis of the spine developed in 2 and caused the death of 1 of them. Spread to other pelvic organs occurred in a further case, in 2 other instances active pulmonary tuberculosis was found to have developed, the condition being confirmed by X-ray examination. The time elapsing between dismissal from hospital and discovery of the

spread ranged from 1 to 4 years (average 2.4 years). The patient with extensive tuberculosis limited to the uterus did not show any evidence of spread of the tuberculous process.

Healed cases. In the literature, when healing of uterine tuberculosis is said to have occurred, this statement appears to have been based only on clinical grounds in most of the cases, and on histological grounds in the remainder. The only exception to this statement is Hedley's¹⁰⁵ case of uterine tuberculosis, in which guinea-pig inoculation with endometrium was subsequently found to be negative. A study of the present series will show that it is not possible to regard a case of uterine tuberculosis as healed on histological or clinical grounds alone. For satisfactory proof of healing a series of negative histological and guinea-pig results over a considerable period of time is probably necessary. If possible, the biopsies should be made towards the end of the menstrual cycle and serial sections of the tissue removed should be cut.

Possibility of spontaneous healing. The possibility of spontaneous healing of tuberculosis of the endometrium must be considered in assessing the prognosis in this condition. Murphy¹ denies that this can occur, but is obviously speaking of the gross type of uterine tuberculosis. Several writers, on the other hand, are of the opinion that spontaneous healing is possible. Benthin,¹⁰⁶ Daniel,³ Gerich,⁴⁰ Rochat,¹⁰ Schroder,¹⁰⁶ Daniel³ quotes several authors who have reported cases in which a healed tuberculous nodule was found in the uterus at operation for prolapse. Four cases in the present series gave negative guinea-pig inoculation and negative histology and may possibly be regarded as examples of spontaneous healing. In these cases only endometrial biopsy had been performed and not full curettage, and the

negative findings were in only 1 specimen from each case, so that the diagnosis of healing is not at all well substantiated

Possibility of cure following curettage
A number of writers have stated that tuberculosis limited to the endometrium may be cured by curettage Brocq,¹⁰⁹ Daniel,³ Foster,¹¹⁰ Goodall,²² Halbertsma,¹¹¹ Hedley,¹⁰⁵ Jameson,⁵ Kroemer,²⁵ Munchmeyer,¹¹² Muret,⁵⁸ Reinhart and Moore,¹¹³ Rochat,¹⁰⁷ Schroder,¹¹⁴ Simmonds,¹⁵ Sipfel,¹¹ Solomons,¹¹⁶ Tourneau,¹¹⁷ Vogt,⁶⁰ Walther.¹¹⁸ Two cases in the present series may possibly be of this type, but this is certainly doubtful because in one instance guinea-pig inoculation was performed only 6 weeks after the initial curettage, and in the other, active pulmonary tuberculosis was found at the follow-up. In each of these cases histological examination and guinea-pig inoculation with tissue removed at biopsy were negative

Possibility of Cure Following Other Forms of Treatment

(a) Hysterectomy with conservation of the appendages was carried out in 1 of the present cases, the patient later developed spinal tuberculosis

(b) Salpingectomy conserving the uterus and ovaries was not performed in any case, the theoretical purpose of such a procedure would be to remove the potential source of reinfection and to leave menstruation to shed off the existing endometrial lesions

(c) Deep X-ray therapy causing cessation of menstruation and consequently a radical functional alteration of the endometrium, was employed in 1 case, when followed up, the patient was well and evidence of spread to other organs was not found

SUMMARY

Three main varieties of tuberculosis of the endometrium are recognized. The first

is quite common and forms merely a trifling part of a widespread genital tuberculosis. The second type is rare and the tuberculous lesions are very gross but are limited to the uterine body. In the third type, which is also confined to the body of the uterus, the infection produces only small, isolated tubercles in the endometrium. The findings of the present investigation show that this third type is relatively common.

In 6,385 specimens in which the endometrium was examined histologically, tuberculosis was found in 11 per cent. The tuberculous specimens were obtained from 58 cases, 24 of which were of the first type, 1 of the second and 33 of the third. The second and third groups form the subject of the present study. In all 34 cases the diagnosis was unsuspected before operation.

The primary complaint was sterility in 24 cases, uterine bleeding in 9 and vaginal discharge in 1. The finding of tuberculosis in about 5 per cent of patients complaining of sterility demonstrates the necessity for careful histological examination of the endometrium in all such cases. The chances of finding tuberculous lesions in the endometrium probably increase slightly towards the end of the menstrual cycle. Twenty sterility patients had tubal insufflation performed, and the Fallopian tubes were found to be blocked in 16 of these. In 5 out of 16 sterility cases in which the endometrium was removed premenstrually, a periodic or total anovulatory cycle was found.

In an average follow-up of 3 years, pregnancy had not occurred in any of the 28 patients traced. Gross spread to other pelvic organs was found once in 25 patients examined vaginally. Tuberculosis of the spine had developed in 2 other instances. An X-ray examination of the chest was made in 17 cases, and evidence of tuberculous disease was found 4 times.

In 16 cases injection of a guinea-pig with tissue removed by endometrial biopsy was

carried out, simultaneous histological examination being made when possible. Tuberculosis developed in 10 of the 16 animals. Guinea-pig inoculation was found to be a more accurate test of activity than histological examination.

The prognosis in such cases must be guarded.

Since completing this study 1285 specimens of endometrium have been examined histologically and tuberculosis has been found 27 times (2.1 per cent). These figures are in reasonable agreement with the present findings.

I should like to express my thanks to Dr H. L. Sheehan for his helpful criticism and advice throughout the investigation. Thanks are also due to Dr McIntyre, Dr Hewitt and Dr Clement for permission to publish these cases, to Dr Hewitt for preparing the microphotographs, to Dr Sharman for access to his sterility records and to Mr W. Wilson for his co-operation and assistance.

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Further Investigations on the Histidine and the Histamine Metabolism in Normal and Pathological Pregnancy *

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IN a recent paper one of us¹ has demonstrated that histidine is a constituent of the urine throughout normal human pregnancy, the amounts excreted ranging between 15 and 50 mgm per cent. Histidinuria appears not to be appreciably affected in cases of mild pre-eclamptic toxæmia but is considerably decreased, or sometimes even absent, in patients suffering from severe pre-eclamptic toxæmia. Further the isolation of histamine from the urine of several patients with toxæmia of pregnancy has been reported, and the suggestion has been made that histamine may possibly be a causative factor of that disease complex. In normal pregnancy urine only traces of histamine have been found.

The object of the present work was to extend these investigations on the histidine and histamine metabolism in pregnancy by the inclusion of a greater number of cases of normal pregnancy, as well as of various types of pregnancy toxæmia.

EXPERIMENTAL PROCEDURE

The excretion of histidine and histamine in the urine of 87 various cases of preg-

nancy has been studied. The urine of each patient has daily been tested for histidine on at least 5 consecutive days by a technique described in a previous communication (1 c). At the same time the isolation of histamine in the form of its flavanate has been attempted by the modified method previously communicated.² It must be pointed out, however, that whereas in the previous experiments large quantities of urine (23 litres to 52 litres) were partly used for the isolation of histamine, in this work only small amounts of urine (3000 c c) have been investigated in this respect.

RESULTS

The results are shown in the following paragraphs.

I NORMAL PREGNANCY CASES

Nineteen patients in the 12th to 42nd weeks of pregnancy were investigated. No albuminuria. Blood-pressure normal. Histidine excretion normal (+ + to + + +). Histamine diflavanate trace.

II PATHOLOGICAL CASES

A NON-TOXAEMIC CASES

1 Organic Heart Disease

Patient No 1 22 weeks of pregnancy 3 para
No albumin in the urine Blood-pressure 100/80

* The substance of this paper was reported at a meeting of the Biochemical Society in Glasgow on June 6th, 1942.

† In receipt of a full time research grant from the Medical Research Council.

Histadine + + + Histamine diflavianate trace
 Patient No 2 35 weeks of pregnancy 9 para
 No albumin Blood-pressure, 100/80 Histidine
 + + to + + + Histamine diflavianate trace,

2 Essential hypertension

Patient No 1 23 weeks of pregnancy 6 para
 Albumin trace Blood-pressure, 235/142 -
 260/140 Histidine + + Histamine diflavianate trace

Patient No 2 32 weeks of pregnancy 4 para
 Blood pressure 210/130, 170/110 Albumin +
 Histidine + + Histamine diflavianate trace

3 Anaemia

Patient No 1 24 weeks of gestation 8 para
 No albumin Blood-pressure, 110/70 Histidine
 + + + Histamine diflavianate trace

Patient No 2 34 weeks of pregnancy 0 para
 No albumin Blood-pressure, 110/65 Histidine
 + + Histamine diflavianate trace

4 Pyelitis

Patient No 1 14 weeks of pregnancy 1 para
 Albumin + + Blood-pressure 110/75 Histidine
 + + + Histamine diflavianate trace

Patient No 2 22 weeks of gestation 0 para
 Albumin + Blood-pressure, 110/60 Histidine
 + + Histamine diflavianate trace

Patient No 3 22 weeks of pregnancy 2 para
 Albumin trace Blood-pressure, 80/50 Histidine
 + Histamine diflavianate trace

Patient No 4 26 weeks of gestation 0 para
 Albumin trace Blood-pressure, 90/55 Histidine
 + Histamine diflavianate trace

Patient No 5 28 weeks of pregnancy 0 para
 Albumin trace Blood pressure, 120/70 Histidine
 + + Histamine diflavianate trace

B CASES OF THREATENED ABORTION

Patient No 1 10 weeks of pregnancy 0 para
 No albumin Histidine + + + Histamine
 diflavianate trace

Patient No 2 15 weeks of pregnancy 3 para
 1 miscarriage No albumin Histidine + + +
 Histamine diflavianate trace

Patient No 3 11 weeks of pregnancy 3 para
 1 miscarriage No albumin Histidine + to + +
 Histamine diflavianate trace

Patient No 4 13 weeks of pregnancy 3 para
 1 miscarriage No albumin Histidine + +
 Histamine diflavianate trace

Patient No 5 16 weeks of pregnancy 0 para
 No albumin Histidine + Histamine diflavianate trace

Patient No 6 19 weeks of pregnancy 2 para
 1 miscarriage Albumin trace Histidine + to
 + + Histamine diflavianate trace

Patient No 7 21 weeks of pregnancy 0 para
 No albumin Histidine + + + Histamine
 diflavianate trace

Patient No 8 19 weeks of gestation 0 para
 No albumin Histidine + Histamine diflavianate
 49.2 mgm out of 3,000 c c of urine

Patient No 9 24 weeks of gestation 5 para
 No albumin Histidine + + + Histamine
 diflavianate 4.0 mgm out of 3,000 c c of urine

Patient No 10 27 weeks of pregnancy 3 para,
 1 miscarriage No albumin Histidine + + to
 + + + Histamine diflavianate 35.6 mgm out of
 3,000 c c of urine

C TOXAEMIC CASES

1 Cases of Hyperemesis Gravidarum

Patient No 1 12 weeks of pregnancy 0 para
 1 miscarriage Albumin trace Blood pressure
 120/80 Histidine + Histamine diflavianate
 16.68 mgm out of 3,000 c c of urine

Patient No 2 13 weeks of pregnancy 0 para
 Albumin 0 to trace Blood pressure 170/60
 Histidine + + Histamine diflavianate 15.72
 mgm out of 3,000 c c of urine

Patient No 3 12 weeks of pregnancy 1 para
 No albumin Blood pressure, 118/70 Histidine
 + to + + Histamine diflavianate 20.49 mgm
 out of 3,000 c c of urine

Patient No 4 10 weeks of pregnancy 1 para
 No albumin Blood-pressure 90/70 Histidine
 + + to + + + Histamine diflavianate 25.32 mgm
 out of 3,000 c c of urine

Patient No 5 8 weeks of pregnancy 3 para,
 1 miscarriage No albumin Blood pressure, 110/80
 Histidine + + Histamine diflavianate 31.26
 mgm out of 3,000 c c of urine

Patient No 6 11 weeks of pregnancy 1 para
 No albumin Blood pressure, 105/65 Histidine
 + + to + + + Histamine diflavianate 62.76
 mgm out of 3,000 c c of urine

Patient No 7 18 weeks of pregnancy o-para
No albumin Blood pressure, 100/65 Histidine
++ Histamine diflavinate 38.85 mgm out of
3,000 c.c. of urine

Patient No 8 19 weeks of pregnancy o-para
Albumin none to trace Blood-pressure 100/60
Histidine + Histamine diflavinate 30.66 out
of 3,000 c.c. of urine

Patient No 9 13 weeks of pregnancy 2-para
No albumin Blood-pressure 80/50 Histidine
++ to +++ Histamine diflavinate trace

Patient No 10 12 weeks of pregnancy o-para
No albumin Blood-pressure 100/80 Histidine
++ to +++ Histamine diflavinate trace

Patient No 11 9 weeks of pregnancy 3-para
No albumin Blood-pressure 110/70 Histidine
++ to +++ Histamine diflavinate trace

2 Cases of Mild Pre eclamptic Toxaemia

Patient No 1 24 weeks of pregnancy o-para
1 miscarriage No albumin Blood-pressure
150/100 Oedema + Histidine + to ++
Histamine diflavinate 176.7 mgm out of 3,000
c.c. of urine

Patient No 2 31 weeks of pregnancy o-para
Albumin ++ to +++ Blood-pressure 150/110
Oedema + Histidine +, Histamine diflavinate
0.9 mgm out of 3,000 c.c. of urine

Patient No 3 32 weeks of pregnancy o-para
Albumin ++ Blood-pressure, 140/100 Oedema
++ Histidine ++ to +++ Histamine
diflavinate 180.6 mgm out of 3,000 c.c. of urine

Patient No 4 32 weeks of pregnancy o-para
No albumin Blood-pressure, 140/105 No oedema
Histidine ++ to +++ Histamine diflavinate
20.4 mgm out of 3,000 c.c. of urine

Patient No 5 33 weeks pregnant o-para
Albumin trace Blood-pressure, 150/100
Oedema + Histidine + to ++ Histamine
diflavinate trace

Patient No 6 33 weeks pregnant o-para
Albumin + Blood-pressure 130/100 Oedema,
+ Histidine ++ to +++ Histamine diflavinate
136.9 mgm out of 3,000 c.c. of urine

Patient No 7 34 weeks pregnant 1-para
Albumin trace Blood-pressure 150/90 Oedema
++ Histidine ++ Histamine diflavinate
5 mgm out of 3,000 c.c. of urine

Patient No 8 32 weeks pregnant 1-para

No albumin Blood-pressure, 120/80 Oedema
++ Histidine ++ to +++ Histamine
diflavinate 9.7 mgm out of 3,000 c.c. of urine

Patient No 9 36 weeks of pregnancy o-para
Albumin trace Blood-pressure, 140/90 No
oedema Histidine + Histamine diflavinate
23.1 mgm out of 3,000 c.c. of urine

Patient No 10 36 weeks pregnant 1-para No
albumin Blood-pressure 140/110 No oedema
Histidine +++ Histamine diflavinate trace

Patient No 11 37 weeks pregnant o-para
Blood-pressure, 146/114 Oedema ++ Histi-
dine ++ Histamine diflavinate 7.2 mgm
out of 3,000 c.c. of urine

Patient No 12 38 weeks of pregnancy o-para
Albumin + Blood-pressure, 150/110 No
oedema Histidine + Histamine diflavinate
26.2 mgm out of 3,000 c.c. of urine

Patient No 13 38 weeks pregnant o-para
Albumin ++ Blood-pressure, 140/100
Oedema + Histidine ++ Histamine
diflavinate trace

Patient No 14 39 weeks pregnant 2-para No
albumin Blood-pressure 160/105 No oedema
Histidine + to ++ Histamine diflavinate 21.4
mgm out of 3,000 c.c. of urine

Patient No 15 39 weeks pregnant 2-para No
albumin Blood-pressure 140/90 No oedema
Histidine ++ Histamine diflavinate 14.8
mgm out of 3,000 c.c. of urine

Patient No 16 39 weeks pregnant 1-para
Albumin trace Blood-pressure, 130/90 Oedema
+ Histidine ++ Histamine diflavinate
trace

3 Cases of Severe Pre-eclamptic Toxaemia

Patient No 1 24 weeks pregnant o-para
Albumin +++ Blood-pressure 210/110
Oedema +++ Histidine 0 to + Histamine
diflavinate trace

Patient No 2 26 weeks pregnant o-para
1 miscarriage Albumin +++ Blood-pressure
160/100 No oedema Histidine trace to +
Histamine diflavinate trace

Patient No 3 30 weeks pregnant o-para 1
miscarriage Albumin +++ Blood-pressure
180/130 Oedema + Histidine trace Hista-
mine diflavinate faint trace

Patient No 4 32 weeks pregnant o-para
Albumin +++ Blood pressure, 220/160

Oedema + Histidine trace Histamine
disflavanate 0

Patient No 5 32 weeks pregnant 2-para, 2
miscarriages Albumin solid Blood-pressure,
175/110 Oedema ++ Histidine 0 to faint
trace Histamine disflavanate 0

Patient No 6 32 weeks pregnant 0-para
Albumin + Blood pressure 190/110 Oedema
+ Histidine + Histamine disflavanate trace

Patient No 7 34 weeks pregnant 0-para
Albumin ++++ Blood pressure, 180/110
Oedema +++ Histidine 0 to trace Hista-
mine disflavanate trace

Patient No 8 34 weeks pregnant 0-para
Albumin solid Blood-pressure 210/140
Oedema 0 Histidine trace Histamine
disflavanate faint trace

4 Cases of Eclampsia

Patient No 1 29 weeks pregnant 1 para
3 fits before admission to the hospital Albumin
solid Blood pressure, 190/140 Oedema +++
Histidine 0 Histamine disflavanate faint trace

Patient No 2 40 weeks pregnant 0-para
14 fits before admission to the hospital Albumin
solid Blood pressure 165/100 Oedema 0
Histidine 0 Histamine disflavanate 0

D MISCELLANEOUS CASES

1 Diabetes + Pyelitis

Patient No 1 *First pregnancy* 26 weeks pregnant
0 para Albumin + Blood pressure
120/90 Oedema + Histidine +++ Hista-
mine disflavanate 47.7 mgm out of 3,000 c.c. of
urine

Second pregnancy (a) 14 weeks pregnant
1-para Albumin + Blood-pressure 120/80
No oedema Histidine +++ Histamine
disflavanate trace (b) 31 weeks pregnant
Albumin + Blood-pressure 140/85 Slight
oedema Histidine +++ Histamine disflavanate
35.2 mgm out of 3,000 c.c. of urine

2 Thyrotoxicosis

Patient No 1 29 weeks pregnant 0 para No
albumin Blood pressure 110/70 No oedema
Histidine ++ to +++ Histamine disflavanate
215.6 mgm out of 3,000 c.c. of urine

3 Acute Hydræmnia

Patient No 1 24 weeks pregnant 1 para No
albumin Blood-pressure, 115/70 No oedema
Histidine +++ Histamine disflavanate 70.1
mgm out of 3,000 c.c. of urine

4 Cerebral Haemorrhage

Patient No 1 32 weeks pregnant 0-para No
albumin Blood pressure 110/70 Histidine
++ to +++ Histamine disflavanate 13 mgm
out of 3,000 c.c. of urine

5 Peripheral Neuritis

Patient No 1 22 weeks pregnant 0-para No
albumin Blood-pressure, 120/70 Histidine ++
to +++ Histamine disflavanate 84.5 mgm out
of 3,000 c.c. of urine

E PUERPERIUM

1 After Normal Pregnancy

Patient No 1 Histidine ++ to + Hista-
mine disflavanate trace

2 After Severe Pre-eclamptic Toxaemia

Patient No 1 Histidine 0 Histamine
disflavanate trace

Patient No 2 Histidine 0 Histamine
disflavanate faint trace

3 After Eclampsia

Patient No 1 Histidine 0 Histamine
disflavanate faint trace

Patient No 2 Histidine 0 Histamine
disflavanate trace

A consideration of the results obtained confirms the previous findings concerning the histidine and histamine metabolism in normal pregnancy, large amounts of histidine and only traces of histamine having been found in the urine of 19 cases of normal pregnancy in various stages of gestation. When checking the findings in the urine of patients with complicated pregnancy, a clear distinction could be made between toxæmic and non-toxæmic cases. In the latter group which comprised 11 different cases such as organic heart failure, essential hypertension, anaemia and pyelitis, the values for the histidine and

histamine excretion do not, on the whole, differ from the normal, except for some cases of pyelitis, in which the histidine excretion was found to be sometimes diminished

Although in 7 cases of threatened abortion the histidine and histamine excretion was comparable to that in normal pregnancy, 3 others showed a distinct histaminuria, 40, 35.6, and 49.2 mgm histamine diflavinate having been respectively isolated out of 3,000 c.c. of urine

The toxæmic cases could be divided into two groups both differing from cases of normal pregnancy. In the one, containing cases of hyperemesis gravidarum and those classed clinically as mild pre-eclamptic toxæmia, the histidine excretion remained normal or was only slightly diminished and in most cases there was a considerable histaminuria. In the other containing cases of severe pre-eclamptic toxæmia and eclampsia histidine was absent from the urine, or present only in traces, and also histamine was obtained only in traces or it was lacking altogether

The patients suffering from mild pre-eclamptic toxæmia showed an elevated blood-pressure, in most cases there was an albuminuria and also oedema, 11 out of 16 patients were primigravidae

All patients with severe pre-eclamptic toxæmia showed a persistently high blood-pressure, and a considerable albuminuria. Oedema was mostly present. Seven out of 8 investigated patients were primigravidae

One of the 2 eclamptic patients developed 3 fits before admission to the hospital, the other one 14 fits. The albumin excretion in the urine was in both cases very high. Oedema was present only in one patient. The blood-pressure was very much elevated in both patients

Further there were 5 miscellaneous cases which may be especially mentioned. They were cases of diabetes, thyrotoxicosis,

acute hydramnios, cerebral haemorrhage and peripheral neuritis. It may be pointed out that in all those patients the histidine excretion was normal but there was a rather considerable histaminuria (13 to 215 mgm histamine diflavinate out of 3,000 c.c. of urine)

Rather interesting results were obtained in the case of a patient suffering from diabetes who also developed pre-eclamptic toxæmia and pyelitis. The patient was in the 26th week of her first pregnancy when her urine was first tested for histidine and histamine. Whereas the histidine excretion was found to be normal, the histamine elimination was considerably increased when compared with the normal. Shortly after the birth of her first child this patient became pregnant again. This time her urine was at first tested in the 14th week of gestation, the patient having again developed pyelitis but not showing any sign of any toxæmic condition. It was, therefore, not surprising that the histidine and histamine excretion was found to be normal

The urine of this patient was again investigated in the 31st week of the same pregnancy when the patient was re-admitted to the clinic as a case of mild hydramnios. The histidine excretion was normal but there was a distinct histaminuria (35.2 mgm histamine diflavinate out of 3,000 c.c. of urine)

In the puerperia following normal pregnancy decreased amounts of histidine were found in the first days after delivery and also traces of histamine. After the 8th day the excretion of both substances ceased

In 2 cases of severe pre-eclamptic toxæmia no histidine, but traces of histamine were found in the puerperal urine and similar results were obtained in the puerperia of 2 patients who had had eclampsia

DISCUSSION

The evidence presented in this work seems to justify the view expressed in preceding papers that histidine and histamine play a significant part in normal and toxæmic pregnancy. Moreover, the occurrence of both compounds in pregnancy urine may have a diagnostic value since a large drop in the histidine and histamine excretion in the urine makes it possible to differentiate between mild and severe cases of pre-eclamptic toxæmia. This is of importance as it is sometimes difficult for the clinician to make a differential diagnosis in the absence of certain signs and symptoms. The relatively large amounts of histamine found in the urine of patients with thyrotoxicosis, acute hydramnios, peripheral neuritis and cerebral hæmorrhage are of some interest and might be suggestive of those complications of pregnancy being of toxæmic origin. It is, of course, impossible to draw any conclusions from findings in single cases and more work must still be done in this direction.

With regard to the 3 cases of threatened abortion with considerable histaminuria, mentioned above, it may be recalled that there are many possible causes of threatened abortion. It may have been that in these 3 cases toxic factors were concerned although clinically it was not possible to differentiate them from the others.

Commenting on the way in which histamine might arise in the metabolism of pregnant women a suggestion expressed in previous communications³ may here be repeated. In normal as well as in toxæmic pregnancy histamine may be formed from histidine, present in large amounts, by the activity of the enzyme histidine decarboxylase. In normal pregnancy most of the histamine formed is presumably des-

troyed by histaminase, only traces of histamine escaping that fate and being excreted in the urine. It is suggested that in milder toxæmic pregnancy, as in hyperemesis gravidarum, and in mild pre-eclamptic toxæmia, the activity of histaminase may be impaired and more histamine may escape breakdown, and cause various kinds of intoxication. A large amount of histamine, however, seems to be eliminated in the urine. In severe cases of pre-eclamptic toxæmia and in eclampsia a condition may arise in which the activity of the histidine decarboxylase may be increased whereas that of histaminase may be completely inhibited with the result that the whole of the histidine appearing in the metabolism might be converted into histamine which may cause considerable damage to the vital organs, especially to the liver and kidneys. In consequence the damaged kidneys may lose the power of excreting histidine and histamine which thus may be completely retained in the tissues. A vicious circle may thus be caused with the result that the more histamine is formed the less active may become the histaminase because of the arising anoxæmia. Eventually the whole body may be flooded by histamine. Conditions may so develop suggestive of severe pre-eclamptic toxæmia or even eclampsia. From these considerations it appears to be possible that toxæmia of pregnancy may be due at least partly to a disturbance of the metabolism of enzymes responsible for the formation and destruction of histamine. To test this hypothesis investigations concerning the activity of the histidine decarboxylase and histaminase in the blood of women with normal and toxæmic pregnancy have been started and are in progress.

Some tentative support for this suggestion may be claimed from recent works of Marcou,⁴ Werle⁵ and Zeller,⁶ who in

independent papers report on the ability of the serum of pregnant women to destroy histamine. As a result of his studies Zeller even goes so far as to assume that the activity of the histaminase is diminished or even lacking in the serum of patients with hyperemesis gravidarum. This observation is in accord with the findings in cases of hyperemesis gravidarum reported above, in which large amounts of histamine were isolated from the urine.

Finally a suggestion of one of us⁷ may here be recalled. Basing on a statement made by Edlbacher and Zeller⁸ that histamine forms a melanine-like compound when oxidized by histaminase and considering the isolation of histamine from the urine of cases with toxæmia of pregnancy it was then suggested that the pigmentation of the skin occurring in pregnancy might be due to the enzymatic destruction of histamine. In a very recent paper Zeller,⁹ in view of the occurrence of histaminase in pregnancy-blood also assumes the possibility of a connexion between the existence of the histaminase in pregnancy-blood and the development of pigmentation in pregnancy.

SUMMARY

Previous findings concerning the histidine and histamine metabolism in normal pregnancy are confirmed. A clear distinction can be made between toxæmic and non-toxæmic cases. In the latter group the histidine and histamine excretion do not on the whole differ from the normal. The toxæmic cases can be divided into two groups, the one containing cases of hyperemesis gravidarum and mild pre-eclamptic toxæmia with normal or slightly diminished histidine excretion, and considerable histaminuria and the other containing cases of severe pre-eclamptic toxæmia and eclampsia when

histidine and histamine are either present in the urine only in traces or they are lacking altogether.

In a group of different cases of complicated pregnancy with normal histidine excretion but considerable histaminuria a suggestion is made, although with greatest reserve, that these cases may be of toxæmic origin.

The significance of histidine and histamine for normal and pathological pregnancy is considered and the part played by the enzymes responsible for the formation and destruction of histamine is discussed.

We wish to express our gratitude to the chiefs of the wards in the Simpson Memorial Maternity Pavilion, Royal Infirmary, Edinburgh, for the permission to use the clinical material.

We are especially indebted to Professor R. W. Johnstone for his helpful criticism.

Thanks are also due to the medical and nursing staff of the Simpson Memorial Maternity Pavilion for valuable assistance in obtaining the clinical material.

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Prolapse Following Hysterectomy

BY

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THE operation of hysterectomy involves interference with the supports of the vaginal vault, and prolapse might be thought to be a common sequel

A study of the literature shows that there are few references to the occurrence of this complication, indeed a paper directly concerned with the subject has not been discovered

During the period of 2 months 5 cases were observed and details of these cases are given below

CASE I

Aged 62 Five children youngest 24 years All normal deliveries

1913 'Manchester' operation

1923 Perineorrhaphy

1926 Vaginal hysterectomy for endocervicitis

Free from symptoms following the hysterectomy for 10 years until under the strain of sneezing she felt something give way

1936 Examination showed the perineum and anterior vaginal wall were sound but the vault was prolapsed

Treated by removal of sac of enterocele and colpoperineorrhaphy

1937 Recurrence of prolapse treated by obliteration of vagina and perineal repair

1940 No signs of prolapse

CASE II

Aged 44 One child (stillborn) after instrumental delivery 20 years previously

1936 Total hysterectomy for fibromyomata uteri At that time no signs of prolapse 3 months after hysterectomy examination showed a well marked enterocele

Treated by ring pessary with relief

1940 Patient could not be traced

CASE III

Aged 60 Two children, youngest 19 First delivery instrumental

1927 Subtotal hysterectomy for fibromyomata uteri No symptoms of prolapse previously Two years after operation complained of feeling of weight in pelvis

1936 Examination showed a well marked cystocele and prolapse of cervical stump together with a slight rectocele

Treated by anterior colporrhaphy Amputation of the cervix and colpoperineorrhaphy

1940 Slight feeling of weight in pelvis No signs of prolapse

CASE IV

Aged 50 Two children, youngest 11 years All normal deliveries

1932 Subtotal hysterectomy for fibromyomata uteri

Slight prolapse present prior to operation which became much worse after operation

1936 Examination showed complete procidentia of the cervical stump

Treated by anterior colporrhaphy with amputation of the cervical stump and colpoperineorrhaphy with almost complete obliteration of the vagina

1940 No complaints and no signs of prolapse

CASE V

Aged 47 No children

1930 Artificial menopause with radium

1931 Subtotal hysterectomy for fibromyomata uteri

1933 Anterior colporrhaphy and colpoperineorrhaphy for prolapse

1936 Examination showed inversion of vagina with ulcer on site of cervix

Treated by Le Fort operation

1937 Recurrence treated by obliteration of vagina

1938 Free from symptoms and no signs of prolapse

The types of prolapse following hysterectomy must be divided into two groups

A This group includes those cases in which a prolapse, symptomless or otherwise, was present before the hysterectomy was performed, and which subsequent to the hysterectomy became more marked. These cases are mainly rectoceles or cystoceles with no descent of the vaginal vault or cervical stump

An explanation of the symptoms only becoming apparent after the hysterectomy has been performed may be that the uterus is a factor tending to prevent prolapse of the vagina, and also the menopause induced may cause fibrosis of the supports

A factor which in some cases may have disguised the prolapse is that, with a pathological enlargement due to fibroids of the uterus, as with a physiological enlargement due to pregnancy, there is some alleviation of prolapse symptoms coexisting with the uterus rising out of the pelvis

B This group arises primarily after the hysterectomy and the prolapse is of the vaginal vault or cervical stump and is of the enterocele type. The mechanism of this type is that of a pure uterine prolapse in that as the vagina becomes inverted it later separates up the pubocervical fascia with the formation of a cystocele and sometime later the formation of a rectocele

Graves¹ writes that in the early days of abdominal hysterectomy, patients often suffered lifelong discomfort afterwards and it was many years before surgeons realized that most of the evil after-effects were due to a descent of the unsupported cervix

The following tables give the incidence of prolapse following the different types of hysterectomy

TABLE I
Prolapse Following Subtotal Hysterectomy

Author	No of cases	No of cases of prolapse
Read and Bell ²	1739	4
Davidson ³	13	0
Pearse ⁴	1900	17
Culbertson ⁵	Not stated	2
Phaneuf ⁶	Not stated	4

TABLE II
Prolapse Following Total Hysterectomy

Author	No of cases	No of cases of prolapse
Read and Bell	605	0
Davidson	165	1
Culbertson	Not stated	3
Phaneuf	Not stated	2

TABLE III
Prolapse following Vaginal Hysterectomy

Author	No of cases	No of cases of prolapse
Babcock ⁷	200	0 (2 cases with return of prolapse)
Vineberg ⁸	83	0 (4 cases with return of prolapse)

In addition Siddall and Mack,⁹ and Davies and Cusick¹⁰ make no mention of prolapse as an after result of hysterectomy

McEwan¹¹ in his series, mainly subtotal, says that upper vaginal prolapse is cured by the operation

Before any discussion on the type of hysterectomy most likely to be followed by prolapse, a short discussion on the anatomy of prolapse is necessary

There are varied opinions as to whether the vagina is supported by muscle or fascia. Frank¹² divides the vaginal supports into

- (a) *Holding apparatus*—which he likens to the springs of a motor car
 (b) *Supporting apparatus*—which he likens to the shock absorbers

(a) The holding apparatus consists of the pubocervical ligament or fascia, the cardinal ligaments and the utero-sacral ligaments (b) The supporting apparatus consists of the levatores ani with the fascial envelope and the triangular ligament

The holding apparatus controls the upper part of the vagina while the supporting apparatus controls the lower part of the vagina

Bonney¹³ also divides the supports into upper and lower divisions. These subdivisions explain in a satisfactory manner the different manifestations of prolapse, being dependent upon which of the supporting mechanism is injured

In the case of prolapse following abdominal hysterectomy it is only the upper supports that need be considered, since it is only these supports which are interfered with during the operation

There are varied opinions as to the frequency of prolapse, following the different types of hysterectomy

Examination of Tables I, II and III show that, from the figures available, prolapse is found about five times as frequently after subtotal as after total hysterectomy

In subtotal operations the fan-shaped fascia is but little disturbed and it would appear that there should be no increase in the likelihood of prolapse following the operation

However, in spite of the small degree of disturbance to the upper vaginal supports it must be remembered that, as Bonney states, the uterus acts as a deterrent to prolapse

Prolapse can be likened to the inversion of a glove finger with the uterus acting as a piston. Provided that the uterus is in the

normal position of anteversion, the difference in the axes of the uterus and the vagina prevents uterine prolapse

After subtotal hysterectomy there is some disturbance in the relation of the axes of the stump and the vagina which may become aligned thereby favouring a prolapse of the stump. It is easier to invert a cylinder than a cone, and after a subtotal hysterectomy the cervical stump, by keeping the upper part of the vagina open, helps to fashion the upper vagina into a cylinder

This can be advanced as a reason for prolapse being more likely to follow subtotal hysterectomy as in total hysterectomy the absence of the cervical stump favours the formation of the upper vagina into a cone

In total hysterectomy there is a considerable degree of damage done to the vaginal supports and Sloan¹⁴ to obviate this favours coring out the cervix

There are two factors which may act as a safeguard against prolapse following total hysterectomy

There is usually some shortening and reduction of the lumen of the vagina and in addition, in the reformation of the vagina, there is a tendency for it to become cone-shaped. This makes it, for mechanical reasons, less easy for prolapse to ensue

In vaginal hysterectomies one factor must be brought forward as favouring a subsequent prolapse. This operation is often performed for procidentia or when there is vaginal prolapse and a uterus requiring removal for some other cause

Admittedly these cases always have in addition to the hysterectomy some repair of the pelvic supports and the vaginal vault is usually supported by utilizing the broad, round and utero-sacral ligaments

From the few references to the subject found in the literature it appears that prolapse is relatively rare as an after result of hysterectomy. When it is considered that prolapse frequently only manifests itself at

the menopause owing to the loss of tone in the tissues, it is rather surprising that, when so many hysterectomies are performed with the removal of both ovaries, the artificial menopause, so induced, does not increase the likelihood of prolapse ensuing

In the cases quoted there were 3 subtotal hysterectomies followed by prolapse and in the literature there seems to be a greater likelihood of prolapse following the subtotal operation. If it is admitted that there is less disturbance to the supports there must be some other reasons for the cause of the prolapse

The increase may be only apparent, since there are more subtotal operations performed and the total hysterectomies are more frequently performed by surgeons of greater experience. In addition total hysterectomies are performed more frequently in older people and for more grave conditions, and thus the expectation of life may not be so long as that of subtotal hysterectomies, and not long enough for prolapse to occur. The cone versus cylinder theory, previously mentioned, may be an important factor

PREVENTION

In subtotal hysterectomies the cervical stump should be supported by stitching the round ligaments to it in such a manner that the axis of the vagina is not brought forward into the same alignment as the direction of the intra-abdominal pressure

In total hysterectomies, in addition to attaching the round ligaments to the vaginal vault and closing the space between the utero-sacral ligaments, the vagina should be closed in a lateral to lateral manner in order that the lateral ligaments of the vagina may be approximated, thereby forming a more tense sling to the upper vagina

In vaginal hysterectomies, in addition to the support of the broad ligament, which

can be overlapped, a good perineal repair should be performed

TREATMENT

Fletcher Shaw¹⁵ states that the most difficult cases of prolapse to treat are those following hysterectomy. This fact is well shown by Cases I and V. Hall¹⁶ in a discussion following a paper on vaginal hysterectomy given by Kennedy,¹⁷ states that the recurrence of cystocele after vaginal hysterectomy will be troublesome and that there is no operation for it that will make the patient more comfortable. Read and Bell in their cases state that 2 of them were treated by vaginal repair and 2 by ventral fixation of the cervical stump. Ventral fixation of the stump as the sole procedure is unlikely to be of lasting benefit as ventral fixation of the uterus is seldom of any value by itself in the treatment of prolapse. Phaneuf advises colpectomy, either partial or total, with removal of the cervical stump when the prolapse follows a subtotal hysterectomy. Farrar¹⁸ utilizes the mid-portion of the stump of the cervix after dissecting off the mucous membrane, in a modified Watkins inter-position operation

The treatment must depend upon the age of the patient, but any operation to be efficient must make coitus difficult or even impossible. There is always a tendency for recurrence and each subsequent operation becomes more difficult owing to the increase of scar tissue

It is advisable to be radical and to perform a complete colpectomy after the manner of Le Fort

SUMMARY

(1) Five cases of prolapse following hysterectomy have been seen within the space of 2 months

(2) Three of these cases were following a subtotal hysterectomy which corresponds

with the larger number following subtotal hysterectomy noted in the literature

(3) A mechanical reason is advanced for the greater frequency of prolapse following subtotal hysterectomy

(4) Total hysterectomy with reconstruction of the cardinal ligaments by lateral to lateral closure of the vagina is suggested as a method least likely to be followed by prolapse

(5) Almost complete obliteration of the vagina is necessary for a satisfactory result in the treatment of the condition

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Primary Abdominal and Primary Ovarian Pregnancy, with a Report of One Case of Each Variety

BY

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CASES of primary abdominal and primary ovarian pregnancy are always of sufficient interest to merit publication. In regard to the former, Novak¹ makes the following statement: "While the possibility of primary abdominal pregnancy has been discussed for many years, and while a very small number of purported instances have been reported, the majority of authors question its possibility. In no case, so far as I know, has the occurrence of primary implantation upon the abdominal peritoneum been established beyond doubt." Speaking of the etiology of secondary abdominal pregnancies, he says: "The correct explanation of these cases is that the placenta remains attached even though the embryo is extruded through the perforation or the fimbriated orifice. Moreover, the villi begin to grow outwards through the rupture point, so that more and more of the placental area and eventually the entire placenta, may be found outside. This is certainly the correct explanation of nearly all and probably all abdominal pregnancies."

Of ovarian pregnancy Novak says: "While there was until recent years much discussion as to the possibility of ovarian pregnancy, there is no longer any doubt on this point. Not all the cases reported in the literature under this head are based upon acceptable evidence, but a considerable number (about 50) are. The generally accepted criteria of diagnosis, are those

formulated by Spiegelberg: (1) That the Fallopian tube, including the fimbria ovarica, be intact and the former clearly separate from the ovary, (2) that the gestation sac definitely occupies the normal position of the ovary, (3) that the sac be connected with the uterus by the ovarian ligament, (4) that unquestionable ovarian tissue be demonstrable in the walls of the sac.

"The logical explanation of cortical implantation of the egg, (Meyer's common mechanism), would be the great frequency with which endometrium is found in the ovary, due to the differentiating potency of the germinal epithelium."

The alternatives are fertilization within the Graafian follicle, and implantation within the follicle after fertilization outside it.

Wilson and Robins² reviewing the literature up to May, 1941, put the number of admissible primary ovarian pregnancies reported up to that date at 59. Between June, 1941, and November, 1941, 5 more cases have been published by Simard,³ Nicholls,⁴ Eckerson,⁵ Ross and Gledhill⁶ and Curtis.⁷ Including the case now recorded the number up to date appears to be at least 65.

If, as Novak agrees, implantation in an endometrial island in the ovary is accepted as the most logical explanation of primary ovarian pregnancy, it is difficult to see why implantation in an endometrial deposit in the utero-sacral ligament, peritoneum

covering the rectum or sigmoid, or any part of the pelvic cavity for that matter, should not be accepted as the explanation of primary abdominal pregnancy.

The widely differing terminations of ectopic pregnancies in general are well-known. They vary from removal following rupture in the first few weeks, to delivery at term, sometimes even with a live child, as reported by Renner,¹ Nicholls, and others. Or the mummified foetus may be retained unawares for years. "Infection of the macerated foetus may occur, with suppuration, the pus finding its way out through the bladder, the rectum, the vagina, or abdominal wall. Through the fistula are passed, first the broken down fluid placenta, then the soft parts of the foetus and finally the separate bones, by a process of suppuration which may last for years and which the patient may not survive" (DeLee.) Smith is quoted by DeLee as recording the removal of a calcified foetus from a woman 94 years old, 60 years after conception.

The diagnosis in those cases presenting an anomalous menstrual history, followed by signs of rupture and intraperitoneal haemorrhage in the early months is usually easy enough. In the rarer cases in which there has been little, if any, abdominal disturbance the pregnancies may proceed to term without the true state of affairs being recognized until the onset of the so-called false labour, death of the foetus, failure of the "labour" to progress, and deterioration in the mother's condition serve as a warning that all is not well. Or, as is evident from the above references, even the fact of pregnancy may be unsuspected for years.

In considering the treatment of these cases at or near term, the chief difficulty lies in the method of dealing with the placenta. Rauch² quotes Hare's conclusion that it should be left *in situ* in all cases of abdom-

inal pregnancy (when its removal might be difficult, and that the abdomen should be closed without drainage). Hare describes an operation for abdominal pregnancy in 1934 in which the foetus was found in the abdominal cavity and removed. The placenta was attached to several coils of intestine, the uterus, both broad ligaments, and the anterior abdominal wall. It was left *in situ* and the cord cut short. The abdomen was closed without drainage. One year later the same woman was delivered by Caesarean section. Careful inspection showed that the placenta left in the abdomen at the first operation was completely absorbed. DeLee describes the danger from severe haemorrhage which attends the attempt to remove a placenta attached to such organs as the rectum, sigmoid, or small intestines. He too left a placenta *in situ*, but had to re-open the abdomen twice to deal with a cloudy bloody fluid which collected in the abdomen. He also records a case in which "the haemorrhage from vascular adhesions absolutely frustrated all attempts at hemostasis by a skilful surgeon and himself." He concludes by saying that "many cases have been cured by simply removing the foetus and cord, sewing up the sac and leaving the placenta for absorption." There appears to be no doubt that the placenta is an absorbable organ, and that it is far safer to leave it in the abdomen than to run the risk of uncontrollable haemorrhage entailed in attempting its removal.

We record below the particulars of 2 cases, the first of which is, we think, an instance of primary abdominal pregnancy and the second an undoubted primary ovarian pregnancy. We base our diagnosis in the first case on the following points:

The placenta was situated on the lateral and posterior surfaces of the pelvic peritoneum, covering entirely the rectum and recto-sigmoid junction, but it did not ex-

tend forward on to the posterior leaf of the broad ligaments. The uterus, both Fallopian tubes and both ovaries were demonstrated to be perfectly free and mobile and the edges of the placenta had no relation with any of these organs. There were no adhesions in the pelvis. The original site of implantation can only be guessed, but a likely explanation would be an island of endometriosis on one utero-sacral ligament or on the peritoneal surface covering the rectum.

The second case appears to conform to all the criteria of Spiegelberg. The pregnancy was early enough for the relation of the Fallopian tube to be clearly seen, which showed that although the ovary was adherent to the back of the fundus uteri and the peritoneum covering the rectum, the tube itself was entirely free and there were no other adhesions in the pelvis. As will be seen in the case-report the foetus in its sac was demonstrated to be deeply situated in the ovary, and chorionic villi were found to have burrowed deeply into the ovary. The specimen has been presented to the Museum of The Royal College of Obstetricians and Gynaecologists.

PRIMARY ABDOMINAL PREGNANCY

Case Report

The patient, a widow aged 38, had been admitted to a general ward in Mayday Hospital as an acute abdomen and we were asked to see her as she was thought to be a gynaecological case.

The history obtained was that she had had a normal pregnancy and delivery in 1922, there had not been any abortions, but the menstrual periods had been irregular for some time prior to November, 1939, when her last normal menstruation was stated to have occurred. She was examined by her own doctor in March, 1940, when she had a brown loss, but the question of

pregnancy did not appear to have been considered at that time. On May 30th, 1940, she was sent to hospital suffering from acute abdominal pain and a blood-stained vaginal discharge.

Examination showed a rather obese, toxic-looking woman, in considerable abdominal pain. Muscular rigidity was well-marked and there was much tenderness in the sub-umbilical region, where an ill-defined swelling could be palpated. Foetal parts could not be felt. Vaginal examination showed the cervix to be enlarged, very soft, and patulous, and there was a blood-stained discharge. The blood-pressure was 150/90 mm Hg, the urine contained a trace of albumin and there was well-marked oedema of the feet and legs of recent development.

A provisional diagnosis was made of a pregnancy of 26 weeks' duration complicated by toxic accidental haemorrhage. An X-ray confirmed the presence of foetal parts. She was transferred to the Maternity Department.

On June 1st a urea concentration test was performed and a catheter specimen of urine sent to the laboratory with results as shown in table on next page.

During the next 3 days the pain gradually subsided, but the brown discharge did not completely cease. On June 6th she was free from pain. The foetal heart was stated to have been heard on June 4th, but could not be heard on June 6th. Her blood-pressure was 130/84 mm Hg, the urine was clear and the oedema much improved. On June 6th she insisted on taking her discharge against advice, pleading urgent domestic affairs, but promised to return when these had been settled.

She returned 32 days later, under a different name, having in the meantime married her lodger, which explained the "urgent domestic affairs" previously mentioned. On re-admission, her blood-

UREA CONCENTRATION TEST (15 gm Urea)

	Urine volume	Urea per cent	Amount in gm
Before urea	—	1.1	—
One hour after	40 c c	1.23	0.5
Two hours after	52 c c	1.7	0.88
Three hours after	58 c c	1.8	1.04
			2.42

Urine examination Albumin—a faint trace Moderately small numbers of epithelial cells and white blood cells No red cells, casts or organisms
A white cell count showed a leucocytosis of 15 680 per c c

pressure was 140/72 mm Hg, there was no vaginal discharge and her general condition was good. The foetal heart could not be heard. An X-ray showed a foetus lying in the transverse position, and well-marked overlapping of the cranial bones confirmed the diagnosis of foetal death.

On July 13th we examined her under general anaesthesia (gas, oxygen, and ether). The uterus was found to be about 9 inches long, and the foetus was lying above and obviously outside it. It was plain that we were dealing with a case of extra-uterine pregnancy. Our chagrin at not having diagnosed it before was somewhat tempered by the recollection that she had taken her own discharge after only a few days in hospital, and had been out of our observation for almost 5 weeks.

The same afternoon, under spinal analgesia (2.5 c c heavy percain), the abdomen was opened. A macerated foetus was removed from among the small intestines. Its weight was 4 pounds 3 ounces, which, allowing for some days for maceration, meant that the duration of gestation was about 34 weeks. This agrees closely with the date of the last menstrual period 233 days before.

On further exploring the abdomen we found very little evidence of an amniotic sac and there was no free fluid. The uterus was easily exposed, was seen to be freely move-

able, and both ovaries and Fallopian tubes were perfectly normal. The umbilical cord was traced down to the pouch of Douglas, where the placenta was seen to be attached to the rectum, which it entirely covered, and to the lateral and posterior aspects of the pelvic peritoneum. Its lower edge could not be seen, but by palpation it appeared to reach the floor of the pouch of Douglas, but not to extend on to the posterior surface of the broad ligaments. The cord was now ligatured close to the placenta, and removed.

The treatment of the placenta did not require much consideration. It was certain that any attempt to remove it would be fraught with the danger of fatal haemorrhage, apart from that of injury to the rectal wall, and of infection. It was decided to leave it *in situ*, and trust to absorption taking place. The abdomen was therefore closed, but as an immediate precaution a corrugated drain was passed down to the pouch of Douglas, and stitched into the lower end of the incision.

Progress was good for the next 5 days. The drain was removed on the 2nd day, there being only a small amount of serous discharge. On the 5th day she complained of severe pain in the right leg, and in the chest and back. The possibility of a venous thrombosis of the leg, and a pulmonary embolism, immediately entered our minds,

but careful examination failed to show any evidence of thrombosis, the pulse-rate was not raised, and there was not any respiratory embarrassment or cough. Shortly after she vomited a large quantity of undigested food, following which the pain in the chest subsided. Further progress was uncomplicated, and the incision healed satisfactorily.

On August 2nd a pelvic examination was made under general anaesthesia (gas, oxygen, and ether). There was some brownish discharge, the uterus was much smaller, and was noted to be well forward in the pelvis. The lower edge of the placenta could be easily palpated, and felt rather rubbery in consistence. An Aschheim-Zondek test was negative on August 2nd.

She was discharged on August 17th and instructed to attend at the postnatal clinic in a month's time. She did not do so.

Fourteen months later, on October 21st, 1941, she was again referred by her doctor on account of a tender swelling in the lower half of the incision. Enquiry into her history since discharge from hospital showed that she had been well, had not seen any necessity to attend the clinic, and her periods had been regular until October 12th, 1941. On this date she had a profuse period which lasted 5 days, was not attended by pain or the passage of clots, but after it had ceased there was pain in the lower abdomen, followed by the development of the tender swelling in the scar. Abdominal examination showed a red, tender, indu-

rated swelling, involving the lower part of the scar and the surrounding tissues, of the size of a hen's egg.

Vaginal examination showed the uterus to be anteverted, freely moveable, not tender, but slightly enlarged, its length by bimanual palpation being estimated at about $3\frac{3}{4}$ inches. No trace of the placenta could be found, either by vaginal or rectal examination, and the rectal walls felt normal. There had not been any difficulty the bowels since the operation. She was admitted to hospital the next day.

Under general anaesthesia the swelling was first aspirated, a small amount of thin fluid being withdrawn. The swelling was then incised and explored with the finger. A quantity of thick pus was evacuated and a sinus found leading down towards the pelvis. A corrugated drain was inserted. Culture of the pus yielded a small growth of non-haemolytic streptococci.

A good deal of brownish discharge drained from the sinus for the next 2 weeks, but then became serous, and had almost ceased by November 19th.

On November 4th she developed a bacillus coli urinary infection, the urine containing 0.3 per cent of albumin, large numbers of white blood cells, but no red cells or casts. Culture yielded a profuse growth of bacillus coli. The urine became sterile after 4 days' treatment with sulphapyridine. On November 3rd, a urea concentration test was carried out with the following result (15 grm urea)

	Urine volume	Urea per cent	Amount in grm
Before urea	—	1.45	—
One hour after	75 c c	1.35	1.01
Two hours after	84 c c	2.1	1.76
Three hours after	78 c c	2.3	1.79
			4.56

Comparison of this result with that obtained in June 1940, shows that the renal function had considerably improved and could now be regarded as normal

She was discharged at her own request on November 19th, with a small elastoplast dressing on the sinus, from which, however, there was practically no discharge. She was instructed to attend for dressings, but again did not do so, and has not been seen since

PRIMARY OVARIAN PREGNANCY

Case Report

The patient, a married woman aged 31, was first seen at the antenatal clinic on September 24th, 1940. The history obtained was as follows

She had had a normal pregnancy and delivery in 1936. There had not been any abortions. The last period was July 6th, 1940. She felt well until August 26th, since when there had been slight vaginal bleeding every day. The uterus could not be felt by abdominal palpation but she complained of feeling dizzy and ill, and the blood-pressure was 138/100 mm Hg. The urine was clear. She was admitted to hospital the same day.

Examination in the ward revealed a slight dirty-brown loss from the vagina, the cervix was closed, but the uterus could not be felt *per abdomen*. The size of the uterus was not noted nor was any extra-uterine swelling felt. She was treated as a threatened abortion, being kept in bed and given injections of prolonon. The Aschheim-Zondek test was weakly positive on September 30th.

On October 5th she was allowed up and for the next 10 days there was not any loss. The blood-pressure was now 116/86 mm Hg. There had not been any abdominal pain since admission. She was discharged on October 14th, and instructed to attend the clinic.

On November 4th the blood-pressure was 160/102 mm Hg, but the urine was clear and there was not any oedema or headache. She stated that she felt well in the clinic but that she had had slight abdominal pain the day before. As the uterus was still not palpable *per abdomen* we were asked to see her.

Vaginal examination showed a somewhat retroposed uterus, not definitely made out to be enlarged, but behind and above the cervix there was a small mass, the exact size of which could not be defined. A provisional diagnosis of ectopic gestation was made, though the history and findings were somewhat equivocal. Although the amenorrhoea was of more than 16 weeks' duration the size of the uterus and of the mass behind it were smaller than might have been expected, and it is unusual for an ectopic pregnancy to progress so far with so little disturbance. It will be noted that she had not complained of more than slight abdominal pain.

On November 4th, under spinal analgesia (heavy percaine, 2.5 cc), the abdomen was opened. The uterus was found to be slightly enlarged. The left ovary was enlarged to the size of a tangerine, much discoloured with haemorrhage, and was firmly adherent to the posterior aspect of the fundus. The anterior wall of the rectum was adherent to the posterior surface of the ovary. The rectum was easily separated but some difficulty was met in freeing the ovary from the uterus, during which there was free bleeding from the surface of the uterus. The left ovary and Fallopian tube were excised. Before closing the abdomen a small gauze pack was placed against the site of attachment to the uterus, which was still oozing, the end of the pack being brought out at the lower end of the incision. The pack was removed after 48 hours. Recovery was uneventful.

A small window was cut into the ovary

which exposed a foetus of about 1 inch in length, lying in its sac at a considerable depth in the substance of the ovary

Dr H W Southgate, pathologist to the Croydon County Borough, who examined the specimen, reported "This is a primary ovarian pregnancy—trophoblastic tissue has burrowed deeply into the ovary, with much haemorrhage"

SUMMARY AND DISCUSSION

Two cases are reported, the first of which is thought to be a case of primary abdominal pregnancy, the second conforming to Spiegelberg's criteria for primary ovarian pregnancy

Some references are made to the literature on both conditions. The difficulties and dangers encountered in attempts to remove the placenta in such cases, and the propriety of treating the placenta as an absorbable organ to be left *in situ* with closure of the abdomen, are discussed

It is of interest to note that the first patient had hypertension, albuminuria, and oedema, which, coupled with the abdominal pain and brown discharge, led to the erroneous diagnosis of toxic accidental haemorrhage. The correct diagnosis would, no doubt, have been arrived at sooner had the patient not suddenly left hospital against advice, after a stay of only a few days. The toxæmia associated with the ectopic pregnancy improved even in those few days, and cleared up completely after removal of the foetus, although the placenta was left in the abdomen. The

placenta could not be felt by bimanual examination 14 months later

The patient with the primary ovarian pregnancy, in whom the correct diagnosis was also missed in the first instance, had a hypertension when first seen, which increased during the next 6 weeks. Its relation to the pregnancy, however, is difficult to assess

Both cases are published by courtesy of Dr Oscar M Holden, Medical Officer of Health, County Borough of Croydon, to whom acknowledgments are due

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Puerperal Tetanus, with Report of a Case Following Septic Criminal Abortion

BY

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THE incidence of puerperal tetanus has recently been fully investigated by the Tetanus Committee of the Royal College of Obstetricians and Gynaecologists, the report being published in June, 1941.¹ From the exhaustive enquiries made it seems certain that the death-rate from tetanus following parturition differs very little from that for the female population as a whole, and in both classes, during the 11 years 1927 to 1937, the rate appears to be about 1 in 700,000. The Committee was not able to obtain recent statistics in relation to non-fatal cases of puerperal tetanus. The Report quotes Le Doze, writing in 1936, as having collected 19 cases of puerperal tetanus from French literature, 14 of which followed abortion.

In August, 1941, Maclean and Challen² reported a case of puerperal tetanus following delivery by the forceps, followed by perineal repair. In their study of the literature these authors failed to find any reference to the condition in the British Isles, but quoted passages from several articles about its incidence in other parts of the world, notably America, China, France, Germany, and India. In 1934,³ and again in 1941,⁴ I described the appalling conditions under which the majority of cases of childbirth are conducted in India, and referred in both articles to the incidence of puerperal tetanus in the Indian State in which I worked for 6 years. These conditions must be particularly favourable

to infection by *b. tetani*. The most favoured material for making floors in the cultivators' dwellings is a mixture of mud, straw, and manure. The clothing of both patient and midwife are soil-stained. The "labour-bed" is often made up of dirty remnants found about the hut, and delivery conducted on this heap of noisome rags placed on the floor. The methods of the native midwives are as conducive to infection as are the conditions under which the labours are conducted. Without doubt many Indian women die every year from undiagnosed and untreated puerperal tetanus.

I record below the particulars of a case of post-abortion tetanus which was under my care in 1941. Before giving the clinical details, however, I would refer to some of the conditions and problems I have encountered in the past 7 years, during which time nearly 1,000 cases of abortion have passed through my hands.

"Reliable statistical information regarding the prevalence of abortion in England is practically non-existent."⁵ This statement applies with even greater force to the incidence of criminal abortion. It is probably true that most cases of threatened abortion which are admitted to hospital are in women who genuinely desire the pregnancy to continue, and many of the patients will have already, even at this early stage, sought advice from their own doctors, antenatal clinics, or midwives. In such cases interference is very unlikely

It is probably equally true that most incomplete abortions admitted to hospital, and especially those in which several days or even weeks have passed since the first stage of the abortion occurred, or in which the condition of the patient has become serious before medical advice or admission to hospital has been sought, are due to illegal attempts to terminate the pregnancy. The fear that enquiries may be made into the possibility of such interference keeps them out of hospital until supplanted by the greater fear that their lives may be in danger, or until relatives or friends, alarmed at the patient's condition, take the responsibility of calling in medical advice. Such cases are often gravely ill when first seen. Some have had haemorrhages severe enough to reduce their haemoglobin to between 20 and 30 per cent, and the first step in their treatment must be blood transfusion.

Many are admitted with high temperatures, offensive lochia, and well-established pelvic inflammatory disease which may have already reached the stage of pus-formation, either in the Fallopian tubes or the pouch of Douglas. Others, and these are the worst types, have developed septicaemia in addition to the local pelvic condition. Three cases due to *b. Welchii* infection died within 18 hours, 36 hours, and 3 days of admission. The latter case had almost complete suppression of urine, which was almost black from methaemoglobin, and her blood urea was 360 mg per 100 c.c. Her body became plum-coloured before death, and autopsy showed all the organs, especially the liver, kidneys, heart, and uterus, to be markedly emphysematous.

Another case died under very similar conditions. Apart from the pelvic condition, there had been practically complete suppression of urine for 36 hours before admission, and during the next 24 hours only

30 c.c. of urine was obtained by catheter, none being passed naturally. This urine was heavily stained with blood pigment, but there were no red cells. The blood urea on admission was 248 mg per 100 c.c. Culture of the urine grew *b. Welchii*. All the known means were tried in an effort to re-establish the urinary function, including intravenous injections of 20 per cent saline, 10 per cent sulphate of magnesia and 50 per cent sucrose, but without success. The blood urea rose to 329 mg per 100 c.c. and death occurred on the 6th day after admission.

Two other fatal cases occurred, in which the clinical findings were quite different from the above. One had been under treatment by her own doctor for 10 days before admission. A large mass of placenta was removed from the uterus on the day following admission, but in spite of intrauterine glycerine and sulphapyridine the temperature continued to rise, small pleural effusions developed, two blood cultures yielded profuse growths of *staphylococcus aureus*, and she died a month after admission. The other patient had been ill for nearly 3 weeks before admission, during which time she had not had any medical attention. When I first saw her she was emaciated and evidently in the last stages of a general septicaemia, with peritonitis and a large pelvic abscess which burst through the posterior fornix just before I examined her. She died 36 hours after admission. The infection in this case was probably streptococcal, though we did not have the opportunity to prove it.

In yet another instance, in which the patient died within 12 hours of admission, autopsy revealed two perforations in the uterus, one in the posterior wall just above the cervix, which was evidently several days old, and another almost at the top of the fundus, obviously quite recent, which was, without a doubt, the cause of the shock.

from which she died. The patient denied any attempt at interference. It was, in a sense, very fortunate that my assistant was only able to make a limited digital examination in the ward, in doing which the finger was not even passed through the os, because during the subsequent enquiry the husband's legal representative made a suggestion which appeared to insinuate that the perforations might have been made in hospital. Had the woman lived long enough the uterus would probably have been explored in the usual way, some form of instrumentation would have been necessary, and it might then have been very difficult indeed to prove that the perforations were not made in hospital.

Among the cases which have recovered, many instances of bacillus coli infection have been seen, most of them localized to the uterus, a number with bilateral salpingitis, pelvic peritonitis and abscess formation necessitating drainage through the posterior fornix, and several with a definite bacillus coli septicaemia, the organisms being recovered from the blood. Apart from these, a common sequel, which generally appears about the 10th day, has been thrombosis of the veins of the pelvis and legs, entailing many weeks of hospitalization, and continued ill-health for months.

During the course of treatment of these cases, I have had many admissions of interference, most of them carried out by the patients themselves, some by abortionists. The methods adopted by the patients have been large doses of aperients, abortifacient pills, douches used in various ways, some very hot, some cold, some only vaginal, others definitely injected into the uterine cavity (whereby great and sometimes fatal shock may be produced), slippery elm bark in many instances, and in one case a celluloid hair slide about 4 inches long, which, instead of entering the uterine cavity

as doubtless intended, was pushed through the anterior vaginal wall and the base of the bladder into the vesical cavity. The result was a purulent cystitis, a peri-vesical extra-peritoneal abscess which was drained supra-pubically, and a *b. coli* septicaemia proved by blood culture. The patient had persistently denied interference, and the hairslide was only discovered after prolonged search with the cystoscope as it was covered with purulent phosphatic deposit, and its removal was even more difficult. A 3 months' foetus and placenta were passed a week after the supra-pubic drainage, and the patient recovered after an illness lasting over 8 weeks.

In the cases in which abortionists were known to have been concerned, laminaria tents were used in one (this case recovered from a *b. Welchii* infection and the abortionist was convicted), slippery elm bark was used in one fatal case of probable streptococcal peritonitis and septicaemia and one case of non-fatal *b. coli* septicaemia (in these cases also the abortionist responsible for both was convicted).

The object of the above somewhat long story is to give a fairly full picture of the state of affairs in regard to abortion, more particularly of the criminal type. When one considers the septic condition of the various instruments used, and the unfavorable circumstances in which the attempts are made, it is remarkable that post-abortion tetanus is so rare.

REPORT OF A CASE OF TETANUS FOLLOWING SEPTIC CRIMINAL ABORTION

The patient, a married woman of 24 years, was admitted to Mayday Hospital on March 26th, 1941, with a history of having aborted a 4 months' foetus and part of the placenta the day before. She admitted having procured the abortion by daily douching for a month, using a dettol solution and a Higginson's syringe

On admission the temperature was 101°F, the pulse-rate 110. The abdomen was distended, and tender in the suprapubic region and both iliac fossae. The uterus was enlarged and very tender on movement and the cervix was open. She was notified as a case of puerperal pyrexia.

On March 27th, 1941, a full blood-count was performed

Haemoglobin	60 per cent
Red blood corpuscles	2 940 000 per c c
Colour index	1.03
White blood corpuscles	9 120 per c c

Differential count

N Polymorphs	91.5 per cent
Lymphocytes	6.0 "
Monocytes	2.0 "
Basophils	0.5 "
	100.0

On March 27th, 1941, the temperature was 102.2°F, and on March 28th, 1941, the uterus was explored under general anaesthesia. A large mass of foul-smelling placental tissue was evacuated by ovum forceps after digital separation, the uterine cavity washed out with dettol solution, and packed with gauze soaked in sterile glycerine. A large mass was felt in the left tubal region. Sulphapyridine had been given from the day of admission and this was continued. The pack was removed after 24 hours, when the temperature was 99.0°F, and it became normal the next day. Her progress was uneven until the 9th day (April 4th, 1941), when she complained of being unable to open her mouth. On examination there was well-marked trismus and some stiffness of the muscles of the back and shoulders. There were no enlarged cervical glands and no carious teeth.

She was diagnosed as clinical tetanus and transferred to the medical side for treatment.

I am indebted to Mr C F Swinton, Medical Superintendent of Mayday Hospital, for the following notes as to further progress and treatment.

April 6th, 1941. Marked trismus with painful spasms of masseters. Marked stiffness of posterior cervical and dorsal erector spinae muscles. Temperature normal. Pulse 90. Lochia slight brown discharge.

Treatment

Anti-tetanic serum	30,000 I U	intrathecal
	40,000 "	intravenous
	30,000	intramuscular
	20,000	subcutaneous

April 7th. Conscious and mentally quite alert but restless. Complains of pain in back of neck and shoulders and of periodic pulling sensation from neck downwards through chest. Trismus marked also stiffness of posterior cervical and dorsal spinal muscles. Generalized headache. Temperature 102°F. Vomited 5 times. Some rigidity of abdominal recti muscles. No respiratory distress, cyanosis or rigors. Can flex and extend limbs normally. Plantar reflexes flexor. Can only just separate teeth. Head retraction.

Treatment

Anti-tetanic serum	20,000 I U	intrathecal
	40,000	intravenous
	20,000	intramuscular

April 8th. Delirious at times. Incontinence of urine. Cannot part teeth. Back stiff. Occasional spasms of muscles of trunk and abdomen.

Treatment

Anti-tetanic serum	30,000 I U	intrathecal
	70,000	intravenous

On this evening she had several generalized clonic spasms of a few seconds duration. Mentally alert.

April 9th. Mentally clear. No vomiting. Not incontinent. Jaw and neck stiffness as before.

Treatment

Anti-tetanic serum	30,000 I U	intrathecal
	70,000	intravenous

April 10th. Jaw and neck stiffness as before. Spasms of abdominal muscles 2 to 3 times an hour.

and had 6 generalized spasms during the past 24 hours

Treatment

Anti-tetanic serum 30,000 I U intrathecal
70,000 „ intravenous

April 11th Given Avertin, 5 jcc at 1 a m Still drowsy at 1 p m , after sleeping well No spasms Neck and jaw stiffness as before Avertin repeated at 9 p m

Treatment

Anti-tetanic serum 40 000 I U intravenous
60 000 „ intramuscular

Avertin as stated

April 12th Slept till 7 a m Less neck stiffness Took food well Generalized spasm in afternoon, and two attacks of localized spasm during night Avertin given at 2 45 p m and 1 15 a m , but did not retain either

Treatment

Anti-tetanic serum 40 000 I U intravenous
60 000 „ intramuscular

Avertin as stated (not retained)

April 13th Alert No spasms but has a generalized urticarial rash Avertin given at 12 15 p m , slept till 8 p m

Treatment

Anti-tetanic serum 40 000 I U intravenous
60,000 „ intramuscular

Avertin as stated Morphine gr 1/6, 11 p m

April 14th Occasional spasms only during morning but had two generalized spasms each lasting a few seconds during afternoon Avertin at 10 p m

Treatment

Anti-tetanic serum 40,000 I U intravenous
60,000 „ intramuscular

Avertin as stated

April 15th Frequent masseteric spasms Bit her tongue Several general spasms of 1 to 2 seconds each with slight cyanosis

Treatment

Anti-tetanic serum 40 000 I U intravenous
60,000 „ intramuscular

April 18th General condition and colour good Gets about 3 jaw spasms in 24 hours Much trismus still, and some neck stiffness

April 19th Five jaw spasms lasting a few seconds each

April 23rd About 2 jaw spasms in 24 hours during past few days Neck still a little stiff but back and abdominal muscles not tonic

April 28th No spasms for past 4 days Can open mouth 75 per cent of full No other symptoms

May 7th No symptoms for past week Up and about Recommended for discharge

SUMMARY AND DISCUSSION

A case of tetanus following self-induced septic abortion is reported The abortion was admitted to have been procured by douching with dettol solution every day for a month, using a Higginson's syringe with a bone nozzle, the whole of the nozzle being introduced into the vagina She stated she never bled while douching It will be noted that though she stated she had passed the foetus and part of the placenta the day before admission, she already had a high temperature and rapid pulse when admitted, and the placenta was very foul-smelling when removed 2 days later The date given for the passage of the foetus may not have been correct

Some reference to the literature on puerperal tetanus is made, and the condition of some of the patients comprising nearly 1,000 abortions treated during the past 7 years is described Although many patients are already septic on admission, and many abortions are admittedly criminally induced in circumstances highly conducive to a variety of infections, the incidence of infection with b tetanus is certainly very rare in this country

In the case now reported the question arises as to when, and by what means, the infection with b tetanus was conveyed The incubation period of tetanus is stated to be 2 to 14 days, but it may be longer, and as a rule a long incubation period means a more

favourable prognosis.⁶ Usually the spores gain entry through abrasions or wounds, which may be so minute as to escape detection. In this case neither wounds or abrasions were seen on the vaginal walls or cervix but the placental site was the obvious port of entry. Spores could have been introduced at any time during the use of the Higginson's syringe, and although a dettol solution was used this would be very unlikely to have had any effect on tetanus spores, though doubtless it restricted infection by other organisms. The condition of the inner surface of the bulb and tubing of the average Higginson's syringe may well be imagined, and the bone nozzle would be no better.

Apart from the means used by the patient there remain the method of evacuation of the placenta and the dressings used at operation and afterwards in hospital. The placenta was removed by ovum forceps after digital separation, the uterus was washed out with 1 in 40 dettol solution, and then packed with 4 inch gauze soaked in sterilized glycerine. This is the method used by us as a routine in all cases of abortion, and infection at this stage can be dismissed.

The batch of pads from which those used for this patient had been drawn were examined but tetanus spores were not found. This batch had already been used in both gynaecological and maternity cases but this patient alone developed tetanus. Vaginal and cervical smears taken after the disease was established were negative, as might be expected. Definite information might have been obtained had the placenta or the Higginson's syringe been examined. Unfortunately, this was not thought of.

The muscular spasms during the attack were only of moderate severity. There was no true opisthotonus, and the muscles of deglutition were never so affected as to require oesophageal feeding. These facts are in favour of a longer incubation period, and suggest that the infection was conveyed by douching. The early diagnosis and prompt treatment, however, must have reduced the severity of the disease to some extent.

The temperature charts are interesting, for they show that there was pyrexia on the first 4 days of the treatment of the septic abortion, followed by an apyrexial period of 6 days. After tetanus developed there was pyrexia on the next eleven successive days, being above 102°F on 7 occasions. Price refers to the absence of fever as favouring the prognosis.

The total dosage of antitetanic serum administered by all routes was 1,000,000 international units.

The case is published by courtesy of Dr Oscar M. Holden, Medical Officer of Health, County Borough of Croydon, to whom my acknowledgments are due.

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The Prognostic Significance of Rise in Temperature in the Course of Radium Treatment of Cancer of the Cervix

BY

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It has frequently been observed that certain patients, suffering from cancer of the cervix, show a rise of temperature during radium treatment while others do not. This observation has caused a good deal of discussion. According to the predominant opinion the pyrexia is not due to the disease itself, but to some coexistent infection which complicates the disease and its treatment.

The incidence of the pyrexia found by different authors varies.

Ducuing and Negre¹ report that a rise in temperature was present in 80 per cent of their cases before treatment and in 90 per cent of all treated cases. These figures include all cases running a temperature above 37° C (98.6° F) taken rectally. Taking into account those cases only with a rise of temperature to 38° C (100.4° F) before or during treatment it was found that 6 per cent showed rise in temperature before and 46 per cent during the course of treatment. This amounts to 40 per cent of cases with rise of temperature during treatment.

Held² found in his series of 145 cases that 39 per cent had some pyrexia (57 cases).

M. Shiraki³ found that out of 607 cases 229 had a raised temperature after treatment, i.e. 37.7 per cent.

In the present investigation the incidence of pyrexia during and after treatment has been studied in a consecutive series of 909 cases of squamous carcinoma of the cervix, treated in the Marie Curie Hospital during

the years 1925 to 1934 inclusively. This series did not include any case in which there was pyrexia present at the onset of the treatment, as it is the custom to postpone radium treatment until after the temperature has settled to normal.

Out of 909 patients 37.5 per cent (341 cases) were found to have had a temperature of 100° F or more during or after the treatment.

In Table I these 341 cases are subdivided, according to the extent of the carcinoma, into the 4 stages. From Table I it is apparent that more febrile cases occur in the more advanced cases of stage 3 and 4, but by no means is this degree of fever entirely absent in the earlier stages. Thus in the 1st stage cases there are 2 per cent of febrile cases, in the 2nd stage cases 23 per cent, in the 3rd stage cases 40 per cent and in the 4th stage cases 58.7 per cent. It will be noted that although in this series all patients who had a rise of temperature to 100° F are included, even those whose temperature rose to 100° F on a single occasion only, the percentage of febrile cases is relatively low compared with the percentage of febrile cases of certain other centres.

Held has reported on the incidence of pyrexia among his patients classified according to the extent of involvement by the carcinoma. In the 1st stage there were 40 per cent fever cases, in the 2nd stage 29.8 per cent, in the 3rd stage 38.3 per cent

TABLE I
CASES TREATED BETWEEN OCTOBER 1925, AND DECEMBER 1934

Stages	Total number of cases	Pyrexial cases	Percentage of pyrexial cases
1	48	1	2.0
2	201	48	23.8
3	512	205	40.0
4	148	87	58.7
1-4	909	341	37.5

and in the 4th stage 73.3 per cent fever cases. His percentage of fever cases in the 1st stage seems remarkably high and his 2nd stage patients show a higher percentage than ours too, but his series is a small one, comprising only 72 patients in stage 1, 2 and 4 collectively, and 73 patients in stage 3. Only in his 3rd stage group of 73 patients is the incidence of pyrexia approximately the same as found in the present series. However, as Held's statistics comprise for the most part patients in the 3rd stage his average percentage is not much higher than ours.

The statistics of all other authors deal only with the groups collectively and do not specify the percentage number of febrile cases occurring among the patients classified into the 4 stages. The average percentage varies between 37.5 and 40 per cent, that of the Marie Curie Hospital being 37.5 per cent.

It is evident that pyrexia, though a very frequent complication, is not an inevitable symptom in the more advanced stages of the disease.

What is the significance of this complication? Authors differ considerably in the degree of importance they attach to it. While some continue treatment undisturbed in spite of a rise in temperature, others discontinue the treatment.

Meigs and Jaffe⁴ consider that "The tolerance of treatment and the general re-

sponse of the patients have no prognostic significance." This conclusion is not in agreement with our experience, as may be seen from the following analysis of our cases. The present investigation has been carried out to study the relation between the occurrence of pyrexia during the course of treatment and (1) the immediate mortality-rate, and (2) the 5 years survival-rate.

I. Pyrexia and immediate mortality-rate

The following figures can be found in the literature, dealing with mortality after radium treatment of cancer of the cervix.

Schroder 2.7 per cent, Hehrer 6.2 per cent, Regaud 1.6 per cent, Heyman 2.0 per cent, Statistique du Centre anticancer de Toul 3.7 per cent, and Ducuing and Negre 2.8 per cent. In the series of 909 patients treated at The Marie Curie Hospital the immediate mortality was 1.7. Fifteen of these died of septic complications and 2 of pulmonary embolism. These 17 deaths out of a total of 909 cases represent a mortality-rate of 1.8 per cent. Out of the 568 patients without any febrile condition, however, only 2 died immediately after treatment, and it is of interest to note that the cause of death in both these cases was pulmonary embolism. This represents a mortality-rate of 0.3 per cent. On the other hand the 341 patients with pyrexia showed 15 deaths which represents a mortality-rate of 4.3 per cent.

2 Pyrexia and 5 years survival-rate

The effect of fever upon the subsequent course of the disease is also well illustrated by a study of the follow-up records of these

Table II shows the 5-year survival-rate for all cases to be 37·3 per cent. When, however, the afebrile and the febrile cases are considered separately, the respective

TABLE II
CASES TREATED BETWEEN OCTOBER 1925 AND DECEMBER 1934

Stages	Number of cases	Five year survival number	Percentage
1	48	40	83·3
2	201	119	59·2
3	512	168	32·81
4	148	12	8·1
1-4	909	339	37·3

TABLE III
APYREXIAL CASES TREATED BETWEEN OCTOBER 1925, AND DECEMBER 1934

Stages	Number of cases	Five year survival number	Percentage
1	47	40	85·0
2	153	107	69·9
3	307	141	45·9
4	61	10	16·3
1-4	568	298	52·4

TABLE IV
PYREXIAL CASES TREATED BETWEEN OCTOBER 1925 AND DECEMBER 1934

Stages	Number of cases	Five year survival number	Percentage
1	1	—	0
2	48	12	25·0
3	205	27	13·1
4	87	2	2·2
1-4	341	41	12·0

patients, from which it is found that patients who had no rise in temperature during treatment remain free from complaints for longer periods than patients who had

survival-rates are 52·4 per cent and 12 per cent (Table III and IV)

The ultimate prognosis for patients with pyrexia seems to be considerably worse than for those without. The above per-

Table II, III and IV illustrate this obser-

tages are open to a slight correction if it is taken into account that some of these cases with fever are not really suitable for comparison as they did not receive a full course of treatment, owing to the development of fever (Table V)

course of radium treatment Of the remaining 55 patients 23 received a single application only, while 32 received 2 radium applications

Of these 55 patients all died soon after this incomplete treatment, 11 actually dur-

TABLE V

Year	Pyrexial cases receiving a full course of treatment		Pyrexial cases receiving an incomplete course of treatment	
	Number treated	Number dying during course of treatment	Number treated	Number dying during course of treatment
1925	1	—	—	—
1926	14	—	1	—
1927	13	—	5	—
1928	12	—	—	—
1929	20	—	7	1
1930	44	1	11	—
1931	52	1	8	3
1932	46	—	9	3
1933	44	—	7	—
1934	40	2	7	4
Total	286	4	55	11

The full course of radium treatment consisted of 3 applications of radium, an interval of 1 week occurring between the first and the second application, and an interval of 2 weeks between the second and the third application Treatment was not begun so long as the patient's temperature was above normal and it was always interrupted when an abnormal temperature arose during course of treatment It was resumed only when the temperature returned to normal If pyrexia persisted, treatment was either discontinued, or deep X-ray therapy substituted for radium, according to the general condition of the patient

Table V illustrates how often the treatment had to be interrupted because of the occurrence of fever Two hundred and eighty-six patients underwent the full

ing the course of the treatment, 31 within the 1st year after the treatment, 8 before the end of the 2nd year and the remaining 5 patients died before the end of the 3rd year

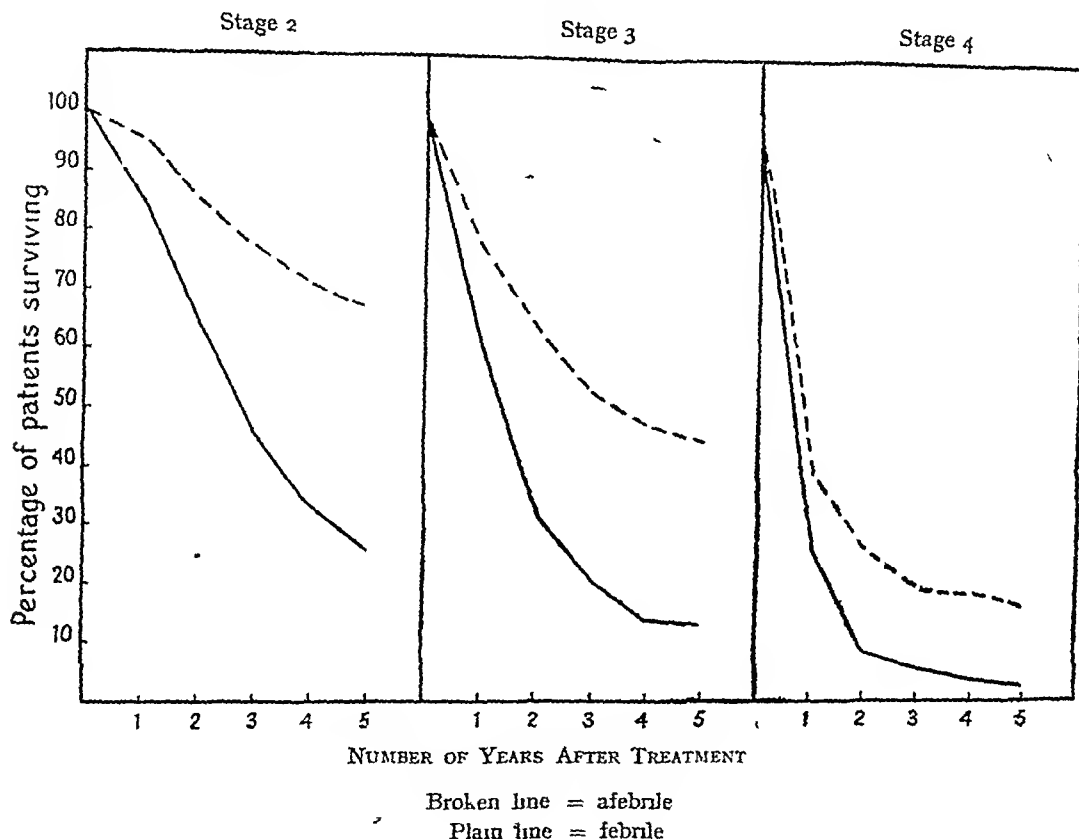
Therefore, if for the purpose of comparison we disregard patients who did not undergo a full course of radium treatment and base the percentage of 5-year survivals on the 286 patients who had the full course, the 5-year survival-rate for pyrexial cases is 14 per cent instead of 12 per cent

From these figures it can be seen clearly that the prognosis is much more serious for those patients who develop a rise in temperature in the course of treatment than for those undergoing treatment without increase in temperature Of the uncomplicated cases 52.4 per cent survive the 5th

year whereas only 14 per cent of cases showing raised temperature survive the 5th year. Further, it is important to note that there is no evidence that the death of these patients was due to direct consequences of the infection which rendered treatment more difficult. Periodical examination of

must interpret any rise in temperature in the course of radium treatment as a grave warning. It not only signifies that the immediate prognosis is bad if treatment has to be discontinued but also that the ultimate prognosis is more uncertain even if a full course of treatment is received.

TABLE VI



the patients did not reveal any grounds for suspecting a febrile or infectious condition, but these patients complained at the "follow-up clinic" sooner than any others of symptoms due either to local extension of the carcinomatous process or symptoms due to secondary growths. In Table VI the steady increase in the number of deaths from 1 year to the next is demonstrated.

From these statistics we learn that we

Although this rise in temperature is more frequent in patients in the more advanced stages of the illness (due no doubt in part at least to lowered resistance of the patient and local necrosis of the growth) nevertheless it is of interest to note that more than half of our patients with advanced carcinoma did not show any rise in temperature. Therefore we must seek to avoid this unfavourable complication, and by so doing

we shall have advanced considerably in the treatment of our patients

The routine study of the leucocyte count has shown that a leucocytosis, which may either precede or quickly follow the rise in temperature is a very frequent occurrence in these pyrexial cases. Held² and Shiraki³ stress the fact that they never found any leucocytosis. In contrast to their experience, we not only find leucocytosis frequently in such cases but also consider the presence of leucocytosis of sufficiently grave significance as to justify postponement of radium application until a normal white cell count has been restored. By this procedure we believe that we can lessen the incidence of pyrexia during treatment and convalescence.

SUMMARY

1 The occurrence of pyrexia in the course of radium treatment in cases of carcinoma of the cervix uteri is an unfavourable development

2 From the group of patients who show a rise of temperature during treatment the total number of deaths in course of treatment is estimated. The persistence of pyrexia results in an increase of the immediate mortality-rate.

3 The 5-year survival-rate of patients showing pyrexia during or immediately after a full course of treatment is lower than that of the remaining patients in the small series of cases here studied.

My thanks are due to Dr. Mary Gilmour, Director of The Marie Curie Hospital, for allowing me to consult the hospital records and for permission to publish these results.

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An Unusual Case of Intraperitoneal Bleeding from a Ruptured Uterine Vein During Pregnancy

BY

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A MRS F P , aged 33, married 2 years and had never been pregnant before, was admitted to the Obstetrical department of the British Postgraduate Medical School with the diagnosis of, perhaps, concealed antepartum haemorrhage on Saturday, March 15th, 1941, about 11 a m

Her last menstrual period was on September 13th, making her 25 weeks pregnant. There had been nothing unusual from her account in her condition until the night prior to admission when at 12 midnight, half an hour after coitus, she was seized with agonizing lower abdominal pain, gripping in type, which made her sweat and roll about the bed, this pain continued all night. A doctor was called and visited her at 9 30 a m , March 15th, and advised her immediate admission to hospital.

On admission, she was obviously shocked and extremely pale, her temperature was 96° F , her pulse-rate 120, of poor volume, thready and very difficult to palpate at the wrist, the respirations were 26 and the blood-pressure 62/48. There was no albumin in the urine.

The abdomen presented an abdominal

tumour the size of a 26 weeks pregnancy which appeared to be just a little larger than the period of amenorrhoea would suggest. This swelling was very tender and thought to be more tense than a normal pregnant uterus. There was some distension of the upper abdomen above the uterine swelling but the tenderness was restricted to the uterus.

The signs of free fluid were not elicited, but the patient was too ill to turn about and as she was undoubtedly bleeding internally further persistence in examination seemed unwarranted.

A very gentle vaginal examination was made and a long cervix felt which did not show any signs of being taken up or of any dilatation. The lower segment of the uterus was not tense and foetal ballotement was identified.

The diagnosis was obscure. Concealed accidental haemorrhage was considered though the period of gestation was early for this. Rupture of the uterus was also considered but did not quite fit the picture.

After resuscitation treatment—morphia, blood transfusion (2 pints) and glucose

saline—which raised the blood-pressure from 62/48 to 108/65, a laparotomy by a sub-umbilical midline incision was performed. This revealed an unusually large quantity of free blood and clot estimated at 3 to 4 pints, in the abdominal cavity. After bowling out the free blood which was citrated and filtered back into the patient's vein, an apparently normal 24 weeks pregnant uterus presented, also normal Fallopian tubes and ovaries.

A further search for intraperitoneal bleeding was made and the original incision enlarged to the ensiform cartilage but nothing abnormal could be found. The uterus, Fallopian tubes and ovaries were then again examined but still the source of bleeding was not detected.

A left transverse incision was then made to expose the spleen and its pedicle. These were examined and also the liver, stomach, mesentery and kidneys, but all appeared normal.

The peritoneal cavity did not seem to be refilling with blood and it was suggested that the abdomen should be closed, as, however, this seemed a defeatist procedure, one further search was made. Finally, a small abraided area was found on the posterior surface of the uterus, it was so slight that it was practically put out of court, but as it was mopped and observed carefully it seemed to ooze. The patient by this time had received about 2 pints of her own blood, this had probably started off the haemorrhage again and with further observation a steady ooze was seen to be maintained at this area. An attempt was made to underpin the bleeding site but this was not satisfactory and, as it was considered possible that the bleeding might be derived from erosion of the uterine wall by chorionic villi from within, a hysterotomy was carried out and a 24 weeks dead foetus removed.

On examining the opened uterus, the placental site was found on the left and the

uterine wall in this area seemed unusually thin. The veins coursing on the surface of the uterus could be seen radiating from this area and one could be traced collapsed but leading to the small orifice on the posterior surface 2 inches from the fundus and slightly to the left of the midline which was no doubt the source of the bleeding. Ergometrine was injected into the uterus which contracted down well, the hysterotomy incision sutured and the abdomen closed.

The patient was returned to the ward with a pulse-rate of 160 and of poor volume but with further intravenous serum her pulse and blood-pressure improved. This progress was maintained until 24 hours after operation when her temperature rose to 101° F and pulse-rate was 140. She was coughing and showed signs of bronchopneumonia, she responded readily, however, to M and B 693 and continuous oxygen by a BLB mask.

By March 18th, that is 3 days after operation, the patient showed marked improvement and made steady progress until she was discharged, ambulant, on April 19th, 1941, that is about 4 weeks later.

The patient has reported as a "follow-up" and her condition to date is excellent.

The interest of the case lies in the unusual source of intraperitoneal bleeding, namely a ruptured uterine vein.

In searching the literature we have found 12 similar cases reported, in 7 cases the source of the bleeding was only discovered at autopsy, the 5 surviving cases are reported as follows.

J. K. Miller¹ in 1928, records a case of a patient 31 weeks pregnant who developed abdominal pain. When seen by him the general condition was good the uterus was sensitive and tense but it lacked the ligneous consistence which one observes in cases of intrauterine concealed haemorrhage.

He made the diagnosis of concealed accidental haemorrhage for which he operated. He found about 1½ pints of free blood in the peritoneal

cavity, he performed a classical Caesarean section but could not find any trace of intramural haemorrhage, so closed the uterine incision.

Finally a brisk venous haemorrhage was observed coming from a dilated vein situated about 1 cm from the right uterine horn behind and toward the midline, this was easily controlled with a single catgut suture.

She was discharged from hospital 22 days after operation.

Modiano,² in 1929, reports a case as follows.

A primigravida, aged 24, 7 months pregnant with a previous history of peritonitis, got out of bed to urinate as she raised herself from the squatting position she was seized with severe abdominal pain. On examination the uterus appeared normal in size for the period of gestation (7½ months) there was tenderness around the uterus and marked guarding of the abdominal wall.

A diagnosis of ruptured uterus or peritonitis secondary to appendicitis was made. On opening the peritoneum 'a tide of blood flooded the field of operation.' With the field clear of blood many adhesions were found between the uterus and neighbouring organs. The incision was enlarged above and below, and an attempt was made to exteriorize the uterus but this was not possible owing to adhesions, but in the process blood was found coming from a large vein low down on the anterior surface of the uterus, a ligature arrested the haemorrhage. The lower part of the uterus was crossed by large varicose veins and many adhesions and it was considered that with further growth of the uterus another vein might be ruptured, so a Caesarean section was performed. The infant died on the 4th day, the patient was discharged on the 22nd day.

H. C. Falks³ in 1931, reported a case in which a woman 26 weeks pregnant, rose from a chair and had severe abdominal pain 7 hours prior to admission to hospital. He apparently made the same intensive search of uterus, Fallopian tubes, ovaries, spleen, liver, kidneys, omentum and mesentery that we made and finally found a small bleeding orifice on the posterior surface of the uterus for which he did a hysterectomy not recognizing the pathology at the time.

Hans Otto Neumann⁴ in 1936 reported a case

of a patient who at term but before the onset of labour, developed signs of severe intra-abdominal bleeding. At a laparotomy he found bleeding from uterine veins low down on the posterior wall of the uterus. He performed a Caesarean section and delivered a live child. He was unable to stop the bleeding as in this case the bleeding vein was low down just above the level of the internal os so he performed a supra-vaginal hysterectomy.

G. Gulowen⁵ in 1939 reports the following cases.

A primigravida aged 31 36 weeks pregnant who had been quite normal up to this time suddenly, while tidying her house was seized with abdominal pain especially in the epigastrium and became pale, dyspnoeic and faint. The doctor who was called thought that the patient had started labour and sent her an hour's journey by car to the maternity home. On arrival there her condition was alarming and she was transferred to a hospital 8 hours after the onset of symptoms.

On examination the patient was pale, restless, with frequent respirations and a rapid pulse. The abdomen was large, distended and rather tender everywhere. The foetal heart was not heard and the position of the foetus could not be determined because of rigidity. There was no vaginal bleeding, the cervix was closed and there was no albumin in the urine.

Premature separation of a normally situated placenta was suspected and it was decided to perform Caesarean section. At operation a large quantity of blood was found in the peritoneal cavity. A stillborn foetus was removed by Caesarean section but intrauterine blood was not found and the placenta was not detached. After suturing up the uterus and removing all blood the source of the haemorrhage was sought in vain. It did not proceed from the liver, spleen, mesentery or intestines. Only after the internal genital organs had been inspected several times without result was it noticed that the haemorrhage came from the right horn of the uterus, where a tear 4 mm long was found in a varicose vein. The bleeding point was ligated. The patient was discharged on the 17th day.

In the case reported by us, there was no doubt that coitus was the final factor in

causing the rupture of the vein, as the history of onset of symptoms was so immediate a sequence. The position of the rupture would coincide in position with the promontory of the sacrum, though subsequent X-ray did not reveal any unusual sharpness of the promontory.

The intensive search required to find the source of the bleeding is emphasized in most of the cases reported above, with a low blood-pressure and a collapsed vein this is readily understood.

We have to thank the Medical Officer of

Health of the London County Council for permission to publish the case.

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The Excretion of Ketosteroids in Human Pregnancy Urine in Relation to the Sex of the Foetus*

BY

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FROM ancient times it has been known that when a cow gives birth to calves, one a male and the other a female, the male will grow into a normal bull and the female may be a freemartin. John Hunter noticed this liability in the horse, ass, sheep and cow. The freemartin is zygotically a female and the external genitalia and mammary glands though modified are usually of female type, but histologically the gonads resemble testes rather than ovaries and there is a tendency for the Wolffian ducts to persist whereas the oviducts are absent or incomplete. William Harvey had observed that with twin pregnancies in equidae and cloven-hooved animals the placentae of the two embryos may become fused. Lillie⁷ in his classical paper showed fusion of the placentae with anastomosis of their blood vessels to be an essential factor in producing the freemartin. Because of the common blood supply, the testicular hormones of the male have free access to the female twin and cause her reproductive organs, including her gonads, to conform towards the male type. This fusion of the placentae, Lillie says, may precede sexual differentiation of the gonads.

When differentiation of the gonads is

complete there is little incompatibility between testis and ovary. This has been shown by transplantation experiments in animals (Steinach,² Moore,³ Finlay⁴), and by uniting in parabiosis animals of different sexes (Morpurgo⁵). Before differentiation the gonads may be profoundly and permanently influenced by sex hormones (Burns^{6-8,9,10}). From these facts it seems that in the embryo freemartin the ovaries are functionless at a time when the testes of her twin brother are already secreting androgen in effective amount. Such a view is supported by histological investigation. Chapin¹¹ examined an embryo freemartin and her twin brother, they were 7.5 cm long. The gonads of the male were 3.5 mm in length and consisted of seminal tubules and interstitial glandular tissue enclosed in a tunica albuginea. In the female the gonads were 2.07 mm in length, contained very few germ cells, and interstitial tissue was not seen.

A condition resembling that of the freemartin may be induced experimentally in amphibia by uniting two larvae so that they acquire a common blood supply. This was done by Witschi and McCurdy¹² with larval frogs and salamanders. In every instance

* A preliminary account of this work was published in *Nature* 1942 cxlv, 300.

in which a male and a female were united in this way the male gonad predominated and modified the ovaries of the female partner so that a condition comparable with that of the freemartin was produced

When a gonad can first be identified in the embryo it appears as a bisexual organ containing a medulla which is the male component, and a cortex which is the female part. Ancel and Bouin¹³ found that the testes of embryo pigs of 30 mm length are composed chiefly of interstitial glandular cells which already contain abundant granules of secretion. No such cells are present in the pig's ovary at this early stage. Allen¹⁴ and Whitehead¹⁵ also recorded a large development of interstitial glandular cells in the testes of embryo pigs of 25 mm. When the embryo pig has attained a length of 35 mm the interstitial cells of the testis involute and are reduced almost to the state of naked nuclei, they recover activity when the embryos are 20 cm long and remain active until birth. In contrast to these findings, Allen did not find interstitial cells in the rabbit's ovary until 45 days after birth. In the male calf, Lillie¹⁶ found interstitial cells in the testis at the beginning of gonadal differentiation, whereas in the calf's ovary they do not appear until shortly before birth. Dantchakoff¹⁷ states that interstitial glandular cells are seen in the gonads of male guinea pigs at a very early stage of development, and that no such cells are seen in the gonads of female embryos.

Such observations seem to show that in embryos the androgenic cells of the male gonad begin to secrete before the ovary has become completely differentiated, and that the ovary does not produce secretion until a much later stage of development. It seems also that the androgens produced in early embryonic life are abundant enough to cause profound and permanent changes in the ovaries of a female twin.

These considerations suggested the desirability of examining the urine of women

in the early period of gestation to discover whether the testes of a male embryo might produce enough androgen to cause a recognizable increase of androgen in the mother's urine. The most likely time for a positive result in such a test would be early in pregnancy in view of the later involution of the androgenic tissue noted by Whitehead and Allen.

Samples of pregnancy urine were obtained from 20 women and the ketosteroids estimated colorimetrically. The method of assay was essentially the same as that given by Callow.¹⁸ Collection of complete 24-hour specimens was found impracticable and the estimations were carried out on samples of morning urine. The values obtained are shown in Table I. The letter M or F denotes the sex of the child as subsequently determined.

The average ketosteroid excretion at 8 weeks for the 14 women bearing a male foetus is 26.2 mgm per litre, while that for the 6 women bearing a female foetus is 14.6 mgm per litre. When account is taken of the wide range of the individual values in these two series it is apparent that this difference between the two mean values is not significant ($t = 1.8$).

The origin of the extra ketosteroid indicated by the seven values for urines from male pregnancies in excess of 20 mgm (mean value, 38.7 mgm) probably lies in the secretion of the embryonic gonads. This probability is strengthened by a consideration of those cases in which assays were carried out later in the pregnancy than 8 weeks. It will be seen that an initially high ketosteroid content tends to fall whereas moderate assays remain substantially unchanged.

Brief clinical reports on these 20 cases are given below. Correlation of these reports with the assay figures do not show any consistent features. The highest values were

obtained from urines of normal pregnancies (cases 1 and 2). Of the two cases treated with Antuitrin-S (cases 6 and 8), one shows the lowest assay of the series and the other one of the highest values obtained.

It must be emphasized that the figures shown in the Table for ketosteroid content do not necessarily indicate the biological androgenic activities of the urines. Caution in making such an assumption is particularly necessary since practically all the urine extracts examined yielded colours with the reagent which were abnormal in type. (For a fuller discussion of the meaning of "abnormal" in this connexion see Callow, *loc cit*). In most cases the absorption of violet light practically equalled that of green light. It is possible that this result is due to the presence in the urine extracts of relatively large quantities of pregnanolones (Marker *et al*)¹⁹ which on treatment with the reagent yield colours showing general absorption particularly towards the violet end of the spectrum.

SUMMARY AND CONCLUSIONS

1. Colorimetric estimations of the ketosteroids were made on 20 human pregnancy urines.

2. In general, no significant difference was found in ketosteroid content between urines from pregnancies bearing a male foetus and those bearing a female foetus.

3. Pregnancies showing especially high urinary ketosteroid (over 20 mgm per litre) terminated in the birth of a male child. In these cases the excess ketosteroid probably originated in the secretion of the embryonic testis.

4. Later assays on urines showing initially high ketosteroid content gave values which tended to the general average value for all the urines examined.

CASE REPORTS

CASE 1 D McG, primigravida age 25. Last menstrual period April 9th, 1938. Previous history nothing abnormal. Normal pregnancy and labour at term. Male child.

CASE 2 N O N primigravida age 27. Last menstrual period March 17th, 1938. Previous history rheumatic fever at 14 and appendicectomy. Normal pregnancy and delivery at term. Male child.

CASE 3 J C 3-para, age 28. Last menstrual period May 9th 1938. Previous history nothing abnormal. Normal pregnancy and labour at term. Female child.

CASE 4 D C, primigravida, age 30. Last menstrual period May 3rd 1938. Previous history seen in 1937 complained of sterility and increasing obesity. Uterus small, periods scanty. Treated with oestrogen and vitamin E. Pregnancy normal. Labour uterine inertia. Normal delivery. Retained placenta manual removal. Female child.

CASE 5 O J primigravida, age 38. Last menstrual period August 11th, 1939. Previous history nothing abnormal. Normal pregnancy labour, and delivery at term. Male child.

CASE 6 T 2 para, age 34. Last menstrual period, August 21st, 1939. History of miscarriages. Bi-weekly injections of Antuitrin-S during present pregnancy. Normal delivery at term. Male child.

CASE 7 C H, primigravida, age 26. Last menstrual period, November 21st, 1939. Previous history large dermoid cyst enucleated from left ovary and resection of cystic right ovary, November 1938. Large cervical mucous polypus and endometrial polypus also removed. Normal pregnancy and delivery at term. Male child.

CASE 8 M P, primipara age 17½. Last menstrual period, October 16, 1938. Previous history scarlet fever when a child. Two miscarriages (1937 and 1938) at 6 and 4 months respectively. Present pregnancy normal. Bi weekly injections of Antuitrin S for 5 months from December 12th, 1939. Normal delivery at term. Male child.

CASE 9 P P primigravida, last menstrual period October 10th 1939. Previous history nothing abnormal. Aborted at the 16th week. Male foetus.

CASE 10 D W, 10-para, age 38. Last menstrual

period, October 10th 1939 Previous history rheumatic fever and severe mitral incompetence Pregnancy terminated March 13th 1940 Female foetus

CASE 11 J McA primigravida age 27 Last menstrual period October 3rd 1939 Previous history laparotomy for fixed retroversion May 1938 Extensive endometriosis of the uterus and pouch of Douglas Seen August 1939 Uterus enlarged retroverted and fixed Last menstrual period, October 3rd, 1939 Pregnancy normal and now no evidence of endometriosis Normal labour at term Male child

CASE 12 H V primigravida age 29 Last menstrual period, October 23rd, 1939 Previous history nothing abnormal Retroverted gravid uterus causing symptoms replaced under anaesthesia Pregnancy otherwise normal Normal delivery at term Female child

CASE 13 P C primigravida age 23 Last menstrual period, February 15th 1940 Previous history appendicectomy otherwise nothing abnormal Manual replacement of a retroverted gravid uterus at the 16th week Pregnancy otherwise normal Normal delivery Male child

CASE 14 B D primigravida age 25 Last menstrual period March 30th 1940 Previous history appendicectomy otherwise nothing abnormal Periods occasionally irregular Pregnancy normal Morning sickness severe Normal delivery Female child

CASE 15 P H primigravida, age 25 last menstrual period July 5th 1941 Previous history nothing abnormal Normal delivery at term Male child

CASE 16 G D 2-para age 38 Last menstrual period, April 13th 1940 Previous history menorrhagia since 1937 Present pregnancy complicated by multiple fibroids Patient had much pain and was in poor health Hysterectomy, July 2nd 1940 Uterus contained a 10 weeks embryo Pathologist reported male foetus

CASE 17 J R primigravida, age 28 Last menstrual period March 15th 1940 Previous history appendicectomy otherwise nothing abnormal Pregnancy and delivery normal Male child

CASE 18 L W 4 para age 41 Last menstrual period July 20th, 1940 Previous history recurrent postpartum haemorrhages in previous labours

Condition of patient poor Hysterotomy and sterilization September 18th, 1940 Male foetus

CASE 19 D H, primigravida, age 26 Last menstrual period, August 9th, 1940 Previous history pulmonary tuberculosis Phrenic avulsion performed 1939 Pregnancy terminated, November 27th, 1940 Male foetus

CASE 20 E A, 5-para, age 32 Last menstrual period December 2nd, 1940 Previous history developed epileptic fits after birth of last child 1½ years ago Fits twice weekly during present pregnancy Pregnancy terminated March 6th, 1941 Pathologist reported female foetus

TABLE I

KETOSTEROID ASSAYS ON URINES OF PREGNANCY

Case	Weeks since last Menstrual period	Ketosteroid (mgm)	
1	8	42.5	M
	14	21.0	
	20	16.0	
2	8	80.0	M
	14	23.0	
	20	20.0	
3	8	14.5	F
	14	15.0	
	20	16.0	
4	8	15.0	F
	14	16.0	
	20	13.0	
5	8	25.6	M
	20	14.3	
6	10	6.4	M
7	8	32.5	M
8	8	35.0	M
	14	21.0	
9	8	25.0	M
10	12	8.7	F
11	8	14.2	M
		15.7	
12	8	12.5	F
13	8	13.5	M
14	8	19.8	F
15	8	18.8	M
16	8	18.2	M
17	8	10.2	M
18	8	30.0	M
19	8	15.4	M
20	8	16.9	F

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FIG 1

A portion of the infiltration zone showing trophoblast invading the wall of a blood vessel

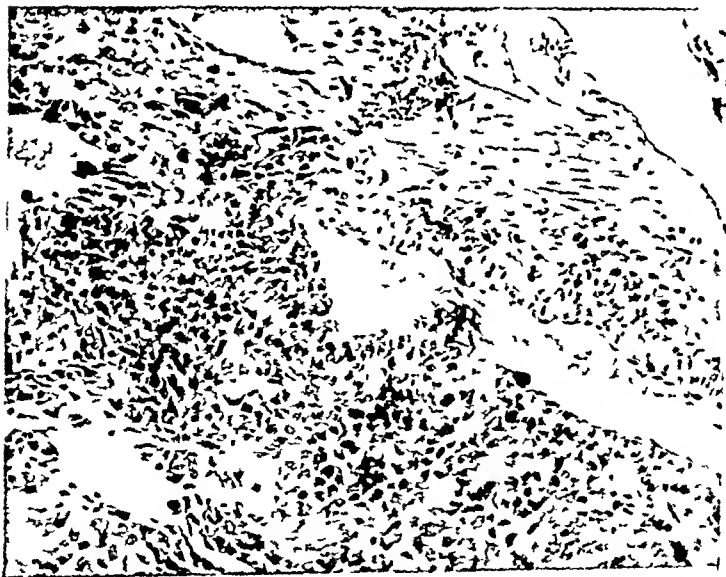


FIG 2

Another portion of the infiltration zone showing a blood vessel the wall of which is replaced by trophoblast and above it some of the tubal muscle

DIVISION of the Zygote Producing Trophoblast Only

BY

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THE absence of all trace of a foetus in most vesicular moles shows that the presence of an embryo is not a necessity for the continued growth of the trophoblast, nor, incidentally, for the continued growth of the connective tissue which forms the core of the vesicular villi although the core of the villus is generally held to derive from the embryonic mesoderm

It is also certain from a consideration of chorio-carcinoma of teratomatous origin that in such abnormal circumstances trophoblast can grow when no embryonic rudiment has ever existed. The question, therefore, arises whether, when a fertilized ovum grafts, it ever happens that the trophoblast alone develops. The following case suggests that it does sometimes happen

The patient having missed 3 periods and believing herself pregnant, for she had hitherto been perfectly regular, had several short attacks of abdominal pain accompanied by slight loss of blood from the vagina. The possibility of extra-uterine gestation was considered, but as the uterus was slightly enlarged and an extra-uterine swelling was not present, the diagnosis inclined to an intra-uterine pregnancy which, after perishing early, had been retained and was now beginning to be expelled. Four days later the patient had a severe attack of abdominal pain and on opening the abdominal cavity it was found full of liquid blood

The left Fallopian tube and both ovaries

were normal. The ampullary end of the right Fallopian tube was ecchymosed out on to the ovario-pelvic ligament but not at all enlarged. There was no gestation-sac, but on the peritoneal surface close to the fimbriae there was an area of shallow erosion about $\frac{1}{2}$ inch in diameter. The blood removed from the peritoneal cavity was searched for the presence of a gestation (molar or otherwise) but none was found.

The Fallopian tube, after removal, was sectioned and the slides showed that the epithelial lining and plicae were normal, as was the muscular wall except at the area of erosion. Here was found a mass of trophoblast (cells and syncytia) in appearance identical with that seen in the infiltration zone of a very early intra-uterine gestation or at the growing edge of a chorio-carcinoma. Villi were not present. Figs 1 and 2

The case was, therefore, one of extra-uterine gestation with primary grafting on the peritoneum. Two explanations are possible. Firstly, that the amenorrhoea was not due to pregnancy and that, after the 3rd period was missed, a fertilized ovum grafted on the peritoneal surface of the Fallopian tube and eroded a vessel within a few days of the grafting, secondly, that the amenorrhoea was caused by fertilization of an ovum, the product of which was a mass of pure trophoblast which, 2½ months later, opened up a vessel. Of these two explanations the second seems to me to be the much more probable.

If it be a fact that on occasions the division

of the Zygote results in trophoblast only a point of practical importance arises, namely that the bulk of such a product will be very much smaller than a normal gestation of the same period, and this will give rise to errors in diagnosis. In the present case, for instance, my opinion was influenced by the thought that an extra-uterine gestation of between 2 and 3 months growth would surely form a tangible extra-uterine swelling, even allowing for those cases known

to all surgeons of experience when an operation reveals, in the Fallopian tube, a blood-mole which must have destroyed the embryo some considerable time before the rupture which determined the operation took place.

In such cases it is obvious that the trophoblast must have continued to erode long after the embryo was dead, and it is not a great step from this happening to erosion without any embryo at all.

Intrapelvic Tuberculosis

BY

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O B E , B A , M D , C M , D S c , F I C S (H o n) , F R C O G

THERE has always been a question whether tuberculosis of the pelvic organs should be treated differently from other types of inflammatory diseases of the pelvis. When looking back over the accumulated experiences, and in particular over those of the last 5 years, one is led to believe that one can now approach this subject rationally, and in the best interests of the afflicted patients. It may be stated categorically that our policy is decidedly conservative, and that it is our conviction that even the gravest types of pelvic tuberculosis are more amenable to recovery than are cases of tuberculosis of other organs, by the general treatment now in vogue for pulmonary and other types of the disease.

INCIDENCE AND PATHOLOGY

Pelvic tuberculosis is fairly common in Canada. It is especially so among the foreign immigrants from warmer climates. It constitutes about 7 per cent of the inflammatory diseases of the pelvis, and is prone to attack those of the second and third decade. It is never fatal *per se*, but patients with pelvic tuberculosis die owing to the ravages of the disease in other parts of the body. It is never primary in the pelvis, being always secondary to a primary focus elsewhere in the body. With the new diagnostic approach, by means of the X-ray, the primary focus can be detected in about 90 per cent of the cases. In the other 10 per cent the clinical diagnosis may

have a larger element of doubt. The disease is most readily suspected in virgins, owing to the absence of infections arising out of married life, or from transmitted venereal disease. In the married, and in the parous woman, the diagnosis is rarely certain without exploration.

Pelvic tuberculosis is essentially a descending disease. Not a single undoubted case of ascending infection has ever been advanced. Even in women married to men with genital tuberculosis, implantation of the disease through intercourse has never been proven. Except in the cases of miliary tuberculosis in which the bacilli are probably blood-borne, pelvic tuberculosis arises out of contamination of the peritoneal cavity by microbes from a primary focus elsewhere in the body. By gravity, aided by peritoneal fluid currents, the microbes settle into the pelvis. When the tubercle bacilli have reached the peritoneal cavity, one of three things may happen. There may develop

- I A general tubercular peritonitis
- II A slight cryptic local pelvic tuberculosis
- III A non-reactive peritoneal cavity invasion

In the diffuse tuberculous peritonitis, the tubercles are usually most abundant in the pelvic region, and grow more sparsely scattered as one ascends in the peritoneal cavity. This peritonitis may be dry or moist, and in the latter case, the quantity of fluid may vary very greatly.

Let us consider briefly each of these three categories. In the dry types there may be no appreciable abdominal cavity because all the juxtaposed surfaces of contiguous organs are joined by a buttery exudate. In both the dry and moist peritonitis the malady is usually of such a nature that the symptoms and abdominal signs put the diagnosis beyond a doubt. When, however, there has been any doubt, exploratory operation has usually followed to confirm the diagnosis. This, of course, is a great aid in any subsequent evolution of the pelvic disease. This primary peritonitis practically always heals spontaneously, and we have learned that the proper course is to close the abdomen as soon as the diagnosis has been confirmed. In the cryptic type of the disease the malady is of such a slight nature that the diagnosis is seldom made, or even suspected, except in retrospect. In the non-reactive cases, the diagnosis of the disease is never made, owing to the absence of peritoneal reaction. The peritoneum is consistently more resistant to tuberculosis than is the mullerian mucosa, but the disease may make itself manifest clinically in the genital tract only at a very much later date than the primary peritoneal involvement. Tubercular peritonitis may heal spontaneously and so completely as to leave no trace of its passage, or a few adhesions may remain between two contiguous peritoneal surfaces, separation of which usually reveals a healed caseous nodule or two, of various sizes, or numerous adhesions may remain as an index of its chronicity.

When any one of these above-mentioned types of peritoneal involvement occurs, one of two sequelae must follow, either the pelvic organs are sufficiently resistant to overcome the contamination, or an infection of the tubal mucosa develops subsequent to the peritoneal involvement. The endosalpinx is the least resistant portion of all the mullerian tract, and involvement of

the uterine mucosa is practically always the result of persistent contaminations from the tubal lumen or tubal lymphatics. Uterine tubercular infections are consequently relatively rare, as compared with tubal involvements, and they usually heal spontaneously when the tubal disease has been removed or has healed spontaneously. The ovary is quite seldom involved. It is never contaminated as an isolated organ, but its involvement is always secondary to that of the Fallopian tube. The capsule of the ovary is practically impervious to the tubercle, except by direct plastic contact, and invasion by contiguity of diseased organs. The few exceptions to this rule are seen when the ruptured Graafian follicles become infected through the operculum of rupture, and give rise to one or more small isolated tuberculous cavities filled with tuberculous fluid.

The common rule, however, is for the tubal mucosa to manifest the disease some time following the peritoneal contamination. The interval between the primary peritoneal invasion and the recognition of the tubal disease may vary within very wide limits. The tubal disease is always bilateral, though both sides may not necessarily be equally involved.

The tubal disease usually takes on two distinct clinical types

I Mucosal disease (a) moist tuberculous pyosalpinx, (b) nodular salpingitis

II Diffuse interstitial salpingitis

In Group I the disease is of a mild nature and its ravages are limited to the endosalpinx. Here, again, we meet with two varieties of the disease, the wet and the dry. The dry is much the more common.

I have seen but 2 pronounced cases of the moist or tuberculous pyosalpinx, though pyosalpinx of a slight nature, of all forms of tuberculous salpingitis may exist. In these 2 cases, which came under my observation when assistant to Professor William

Gardner, the disease affected young girls, one 17 years of age and one 19 years. There was no history of a previous peritonitis, nor could any primary focus be detected by clinical examination. Both had enormous tumours in the hypogastrium. The pre-operative diagnosis was new-growth, probably dermoids. On opening the abdomen the Fallopian tubes were like huge cornucopias. In the first case they measured $10\frac{1}{2}$ inches in circumference, and were 10 inches long, fairly tense and of a yellow-white colour. The other case was very similar, but the Fallopian tubes were not quite so large. The fimbriated end of the Fallopian tubes was characteristic of such cases. There was a marked constriction just at the roots of the fimbriae, as if a tight cord had been tied about it. The fimbriae stood out isolatedly, like turgid digits, and the aperture of the lumen was plugged with a large inspissated caseous mass. There was not a detectable peritoneal adhesion anywhere. In the dry tuberculous salpingitis there is no pyosalpinx, but there are isolated nodules of caseous tubercles about the lumen of the Fallopian tube. They may vary considerably in size, and may be either caseous or calcified. This type is frequently accompanied by adhesions of contiguous peritoneal surfaces, in the midst of which are tuberculous nodules in the same state of healing as those in the tubal mucosa.

In the second group, diffuse interstitial salpingitis, we find Fallopian tubes that may contain a minimum of fluid, frequently grumous, at other times definitely tuberculous, pus, but there are massive diffuse pelvic adhesions, in the midst of which thick hard Fallopian tubes, with infiltrated walls and tubercular nodules, are finally found. The tubal walls are usually so infiltrated that, when cut across after removal, they are rigid, retain their shape, and are very friable. All normal lines of cleavage are lost, and the pelvic organs more or less

fuse into a solid mass. From careful observation of these cases clinically, operatively and pathologically, I am convinced that they are cases of mixed infections, usually the implantation of a tuberculous process upon a previous chronic, simple or specific salpingitis. The two often seem to accentuate their pathological potentialities, producing diffuse infiltrating processes and multiple abscesses in ovaries and between peritoneal folds—the so-called choked pelvis.

It is not to be inferred that the diffuse pelvic inflammatory disease is the product of one continuous process. The pelvic peritoneal cavity is often the victim of repeated invasions from the tubal diseases, and, owing to the chronicity of these processes, the disease may often reach astounding degrees of spread with a paucity of symptoms and a minimum of distress that are quite startling. For peritoneal tolerance to tuberculous is great, and its sensitiveness is awakened only by an acute major insult. Adhesions that are evolved slowly have a power of accommodation that causes surprisingly few symptoms.

The endometrium is relatively seldom involved as compared with the Fallopian tubes. The uterine disease is secondary to the tubal involvement, and its favourite sites are at the cornual end of the uterus, by direct lymphatic extension from the intramural part of the Fallopian tube, and secondly at the shelf of the internal os, where the disease is usually developed by sedimentation.

The reasons why these two sites—namely the cornual uterine mucosa and the region of the internal os, are susceptible to tubercular implantation, has recently been discovered in the research laboratory at St Mary's Hospital. At these two sites the endometrial lining does not take part in the cyclic changes of menstruation and, therefore, unlike the uterine mucosa which is

shed at intervals, these areas have a more or less fixed mucosal epithelium. This greatly favours implantation of disease. At the internal os of the uterus there is quite an appreciable area between the uppermost limit of the cervical mucosa and the part of the uterine mucosa which responds to the ovarian hormonal secretions. This neutral, fixed area has all the histological characters of the uterine mucosa though appreciably thinner than the normal mucosa. It lacks the defensive viscid secretions of the cervical epithelium and lacks also the renewing influences of the cyclic changes of the uterine mucosa. This neutral area is very frequently the seat of cystic disease which leads to partial occlusion of the cervical canal and consequent imperfect drainage of the uterine secretions, thereby producing a certain degree of stasis. This interesting and new subject of research is being dealt with at some length in a paper now in progress upon "The Defensive Mechanism of the Uterus Against Infection."

The uterine musculature is singularly resistant to all types of infection. This applies particularly to tuberculosis. The uterine myometrium was found involved, and that only to a slight degree, in only 2 instances in the numerous cases that have come under careful examination. In both these cases the endometrium was grossly involved in the disease, as were also all the other pelvic mucosal surfaces.

Cervical tuberculosis is relatively rare, and not always easy to diagnose, in that the tubercles are usually atypical and may be simulated by other chronic disease processes. Tuberculous pyometra is quite uncommon, but, nevertheless, well recognized. It nearly always occurs after the menopause.

DIAGNOSIS

The diagnosis of tuberculosis of the pelvis is not easy at any time and may become

extremely difficult, at times impossible, except by exploration. It may readily be confused with subacute or chronic inflammatory disease, both specific and non-specific, peritoneal endometriosis, and malignancy. A painstaking history is of the utmost importance. The history of a tuberculous lesion elsewhere in the body, or the demonstration of this during examination, will be strongly suggestive evidence that the lesion in the pelvis is a secondary development. The history of a previous attack of peritonitis, whether confirmed as tuberculous or not, should be given due consideration. These findings in a virgin practically rule out other septic processes, but cannot exclude endometriosis. In the married and parous woman diagnosis becomes correspondingly more difficult. The history of a recent abortion almost rules out tuberculosis and endometriosis and, therefore, the presumption would be that the pelvic lesion is a septic process. The general opinion is that the skin or temperature reactions, as aids to diagnosis, are all too delicate to be of much value. The frequency with which doubt will surround these cases makes confirmatory exploration inordinately frequent.

TREATMENT

The previous sections have been introduced in order that the present subject may be dealt with comprehensively, for it is felt that so many errors have been made in the handling of these cases that one's own convictions should be told fairly and squarely. Every means at our disposal should be used in order to determine the nature of the disease, for I believe that operation upon pelvic tuberculosis is rarely justifiable if the diagnosis of tuberculosis is certain. Exploratory operation then becomes merely a diagnostic operation, and manipulation should cease as soon as the diagnosis has been confirmed. Now that seems very

simple, but it is not always so. At operation a recent peritoneal disease of a tubercular nature will usually show the peritoneum generally studded with small tubercles, and the diagnosis is seldom further in doubt. Occasionally, malignancy of the peritoneum may take on a close similarity, but as a rule the matter is soon differentiated. But in chronic pelvic tuberculosis the upper peritoneum may be smooth and glistening, the pelvis from above may present a "choked" type of infiltration, the true nature of which is often obscure until one begins to burrow through to the specific organs. Even non-tuberculous cases should not have placed the surgeon in such a questionable position. This, in itself, is a confession of defeat. But such cases will occur with the most wary. As a rule, however, experience teaches us the characteristic nature of the disease, and the type of adhesions is so characteristic that one has soon confirmed one's suspicions.

There are only three diseases which produce adhesions that are in a class by themselves. These are tuberculosis, malignancy and endometriosis. In all other types of adhesions the lines of cleavage are readily found, and one can outline each organ and outline it by blunt hand dissection. This is not true of the three above-mentioned diseases. In these, all lines of cleavage disappear, and two juxtaposed organs become inseparably fused by the infiltrating disease, and in endeavouring to separate fused structures especially the small and large intestines, fistulae readily develop. The sites of endometrial and malignancy adhesions differ from those of tuberculosis, but this may help but little. The recognition of caseous matter or of calcareous nodules practically confirms the diagnosis.

Prior to operation a very good clinical diagnostic aid is found in a certain form of treatment. In tuberculous disease of the pelvis it has been invariably found that the

ordinary heat treatment, so frequently employed with advantage in chronic inflammatory disease, nearly always renders a tuberculous case infinitely more uncomfortable. Unfortunately this applies also to endometriosis and, to a lesser degree, to ovarian malignancy. However, it is of great service, if the disease is definitely one of the infections, in differentiating between an ordinary ascending and a tubercular descending infection.

Is it to be inferred, then, that operation is never indicated in pelvic tubercular disease? That is the desideratum, but that attitude cannot always be adopted. It is infinitely safer to explore than to allow the diagnosis to remain in doubt, for upon certainty, and upon certainty alone, can a rational treatment be adopted, and since so many of the cases must remain in doubt without exploration this procedure must be looked upon as a diagnostic measure, but not a curative one. The inference then is that one should back out of the abdomen as soon as the diagnosis has been confirmed. There are very few exceptions to this rule, though exceptions there must be. As instances of justifiable surgical procedure I have but to quote the two cases of tuberculous pyosalpinx described above. Obviously, one's duty in such cases is excision.

In many instances the abdomen will have been opened under a mistaken diagnosis, and tuberculosis will have been found as a complete surprise.

We wish to emphasize this broad statement, upon which much of our argument hangs, and that is that patients never die of tuberculosis unless surgical intervention has turned a local curable disease into one of grave import. Let me accentuate this dictum.

Cases of very destructive nature have healed spontaneously when, prior to this experience, such a condition would have been thought impossible.

Three years ago I opened the abdomen for the presence of a large mass in the right lower quadrant in a choked pelvis. Tuberculosis was suspected, but one could not exclude an appendicular abscess. The patient was 20 years old and a virgin. Upon opening the abdomen, the peritoneum presented a few tubercles that were diagnostic. The whole pelvis was choked, and on top of this, to the right, lay a thin-walled purulent collection. I aspirated this and removed a small piece for biopsy. The fluid content was almost 3 ounces, turbid, but liquid. Guinea pig test was positive in 6 weeks. The patient's wound healed uneventfully, and she was sent away to a sanatorium for 18 months. Six months after her return she developed a bursitis over the right Poupert's ligament. This was aspirated, definitely tubercular pus was obtained, and a tight pressure bandage was applied after aspiration. On bimanual examination of the pelvis it was impossible to detect the slightest deformity or trace of the former disease. She is now enjoying the best of health. Except some calcified glands on the lung root, a primary focus was not detected.

This case serves to illustrate our experience with these cases. Never have we had to regret conservative diagnostic operation, but surgical enucleation has given us many sad experiences arising out of what we now consider was bad judgment.

The following case illustrates the great curative power of nature and the tragic consequences of radical surgical intervention.

The patient was a woman of 40 years of age. She had been a spinster until 6 weeks previously. She started a motor trip across Canada on her honeymoon and, when 300 miles from Montreal, she began to develop severe abdominal pain. This grew so severe that when 25 miles from the city she had to stop and the ambulance was sent for. Her history was that she had had a severe peritonitis 18 years previously and had been

confined to bed for several months. She had had a lung infection prior to this and it was thought that the pelvic condition was secondary. She was again sent to a sanatorium for a year and had enjoyed excellent health since.

When examined in the hospital she had signs of a general peritonitis, a large mass filled the right lower quadrant, and bimanually this extended down to the right of the uterus, pushing this organ strongly to the left. There was a high fever, chills, high leucocytosis and a rapid sedimentation. Operation was decided upon owing to the uncertainty, and with the possibility that this might be a ruptured pelvic appendix abscess. There were signs of a low grade peritonitis, streptococcal in character and the pelvis was "choked." I burrowed down to find the abscess and drain if necessary. To my great astonishment I found that the appendix, though involved, was merely secondarily, and I opened up a cavity the size of a Californian orange, filled with old tuberculous matter in the right broad ligament. The contents were like old broken up hard mortar which came away in chunks of various sizes. I retired as quickly and as gracefully as I could, after having closed the upper opening of the cavity with omentum.

The patient had a surprisingly smooth recovery for the first 11 days. Then a small bleb appeared in the abdominal wound, 5 days later the whole wound had opened up, 2 days later the parietal peritoneum was visible, studded with small tubercles, 5 days later a fistula developed and the patient died of inanition 6 weeks after the operation.

I had not thought it possible that a pelvic caseous lesion of the size stated could have healed spontaneously. Yet it had and had been quiescent for 18 years. I am equally certain that had I closed the abdomen as soon as I had determined the character

of the disease instead of exploring more widely, the subsequent story would have been a happier one

My earlier experience in handling these cases was not an unqualified success. Many cases developed fistulae and I saw many others in consultation with similar results, and a fistula is about as unfavourable a sequence as one could imagine. On the other hand, the conservative treatment of these cases in the past 10 years has been an almost unqualified success. I have been led to this form of procedure by the knowledge of five facts: firstly, that patients do not die of pelvic tuberculosis if not operated upon, secondly, that when operated upon they are susceptible to secondary infections, thirdly, that heroic surgical treatment in advanced cases is rarely happy and often tragic, fourthly, that most advanced cases of pelvic disease respond surprisingly to general rules

of treatment as laid down for tuberculosis in general, and fifthly, non-interference has the advantage of not producing any deleterious effect upon a primary focus elsewhere in the body.

It can be readily seen that the primary focus of tuberculosis in the body upon which so much stress was laid in the past when operative treatment was the accepted rule, now hardly enters into the discussion when the conservative policy is adopted. The primary focus now becomes the dominant one in the question whether recovery is possible or not, and upon that question hinges the future of the patient. The accepted treatment for the primary focus is in conformity with that advocated for the pelvic lesion. If the primary focus is not demonstrable the treatment should follow the same line as that for demonstrable tuberculosis.

Local Anaesthesia in Vulval and Vaginal Surgery

BY

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FOR gynaecological surgery local anaesthesia is so rarely used in this country, with the exception of Caesarean section, that its value is not appreciated, nor is it realized that its application is extremely easy and, if a few simple rules are observed, almost fool-proof

The term "local anaesthesia" is used in its widest sense, and includes the procedures sometimes referred to as "regional anaesthesia," "field block," and "nerve block" The anaesthetic used has been Novutox, a proprietary preparation containing a solution of Procaine with epinephrine in Ringel's solution, and also quinine derivatives and thymol The solution appears to remain sterile indefinitely, and the duration of the anaesthetic period is longer than that produced by Novocaine alone It has been used in various dilutions from $\frac{1}{2}$ to 1 per cent of Procaine with almost equal success The final choice has been for 1 per cent, as this somewhat reduces the total quantity of fluid to be injected The total amount injected in this series has rarely exceeded 40 c c in a single operation

It should be borne in mind that in addition to anaesthesia, as in abdominal surgery, muscular relaxation also is frequently required This applies to the muscles of the perineum and the pelvic floor in most vaginal plastic operations, and frequently, if access to the cervix is desired, in other operations

ANATOMY

The chief nerve supply of the vulva is from the pudendal nerve, which sends fibres to the whole area from the perianal skin to the clitoris, including the vestibule and urethra The nerve runs in close relation with the artery and vein of the same name, entering the ischio-rectal fossa by crossing the ischial spine In the perineum it is deeply placed in the outer wall of the ischio-rectal fossa and protected by a sheath of fascia At the base of the triangular ligament it divides into its two terminal branches, the perineal and the dorsal nerve of the clitoris The perineal nerve divides again into two, superficial and deep, the former being entirely cutaneous, and both its main branches rapidly becoming superficial to supply the perineum and labia, the deep branch is mainly muscular and supplies the perineal muscles and the anterior parts of the levator ani The second terminal branch of the pudendal, the nerve to the clitoris, runs forward close to the pubic arch, and becomes superficial by piercing the triangular ligament not far from the apex of the arch to reach the clitoris The area of the vestibule around the urethra is supplied by the pudendal nerve, but it is doubtful whether this supply is via the nerve to the clitoris, or the superficial or deep branch of the perineal nerve

In addition the ilio-inguinal nerve sup-

plies branches to the mons veneris and the labia, the genito-crural to the labia, and the small sciatic to the perineum and probably, also, to the posterior area of the labia.

The levator ani receives also muscular nerve fibres on its upper surface from the sacral nerves.

The nerve supply of both the cervix and vagina is a continuation downwards of the uterine plexus, following the course of the cervical and vaginal branches of the uterine artery. There is, however, an area of the posterior vaginal fornix where the sub-epithelial and sub-peritoneal tissues are identical. The nerve endings of the nerves supplying the pouch of Douglas (probably branches of the 3rd and 4th sacral nerves) lie in this tissue.

It is well known that the sensibility of the area under discussion varies enormously in degree. The clitoris and labia minora are exquisitely sensitive to protopathic stimuli, the vaginal epithelium less so, and still less the cervix, the latter may be grasped with bullet or tissue forceps with only slight discomfort to the patient. It is frequently mentioned with apparent surprise that forcible dilatation of the cervical canal is extremely painful. How could it be otherwise? Comparable force applied to any similar organ will produce the same result, but here again sensibility varies in degree. A recently dilated cervix may be dilated again almost to the same diameter without great discomfort. This is true when there has been a recent abortion, and is also noticeable when a radium application inside the uterus is repeated within a week of a former treatment. In the majority of such cases the cervix may be dilated without pain.

TECHNIQUE

It is obvious that the technique of local anaesthesia for gynaecological surgery of the vulva and vagina will vary consider-

ably from case to case. Excision of the vulva requires nerve block of all the nerves mentioned above, but such a complicated procedure is quite unnecessary in the majority of operations.

The pathological condition most frequently seen in gynaecology is genital prolapse in one of its several forms. Of the many varieties of plastic vaginal surgery for its cure, the Fothergill* colporrhaphy has become the operation of choice whenever there is descent of the cervix, and there is no contra-indication to its amputation. The following technique in the use of local anaesthesia is now suggested as a routine for such an operation. It has proved a success in several hundred cases including many different operations, yet this technique is most easily employed when the cervix presents at the vulva, and the value of this form of anaesthesia can be best appreciated during and following colporrhaphy.

The theory of the technique is based on anatomical facts, and the following principles may be stated as reasons for each particular step in the operation. If a comparatively small area (such as the labia) receives sensory nerve fibres from a number of nerves, it is both easier and more successful to infiltrate the tissues with the anaesthetic than to attempt a block of each individual nerve. But when a large area (such as the vagina) receives its nerve supply from a single nerve or nerve plexus, it is preferable to block the nerve rather than infiltrate the tissue.

The ordinary record syringe has been used in all cases, but it is wise to be provided with various sizes, preferably those with finger grips. It will be found that the

* This operation is here correctly named. It is frequently labelled with the incorrect title 'Manchester operation' a misnomer which causes amusement to those with an accurate memory of gynaecology in Manchester 20 years ago.

20 c c size will completely obstruct the view of the cervix, if the vagina is narrow

A point on the perineum $\frac{1}{2}$ to 1 inch antero-lateral to the anus is chosen. Here, with a very fine needle (26 S W G), an intra-dermal vesicle is raised, the needle is then pushed forwards, and the subcutaneous tissue of the anterior margin of the perineum is injected. A larger needle is then used ($21 \times 2\frac{1}{4}$) and is slowly thrust into the perineum through the vesicle to a depth of 2 inches, in a direction at right angles to the skin surface, the anaesthetic being injected as the needle advances and retires. The needle is almost withdrawn, and then directed forwards, but quite superficially, underneath the line of the reflexion of the folds of the labium minus and as far as the anterior extremity of the proposed perineal incision. The procedure is repeated on the other side of the perineum, and about 10 c c of anaesthetic is injected into each. The object of the deep injection is to relax the superficial and deep muscles of the pelvic floor, and to anaesthetize the deep perineal branch of the pudendal nerve.

A vaginal speculum is then inserted, and the cervix grasped with tissue-forceps. The larger of the needles is again used, and the injection is made through the vaginal fornix close to the cervix and immediately lateral to it (at the positions 3 and 9 of a clock). Ten c c of anaesthetic are also injected here. An important consideration is the depth to which the point of the needle must travel. Theoretically it should reach to the level of the cervical internal os, but this distance depends on the length of the cervix, and varies in different cases from one to several inches, and at this stage of the operation it is not possible to make an exact measurement. An attempt is therefore made approximately to estimate the length of the cervix before the dilators are passed.

This completes the routine in most cases, and the operation may begin immediately the last injection is completed.

There are, however, three areas where anaesthesia may be required and will be found not to be perfect when this technique is used. Associated with genital prolapse there may be prolapse or hernia of the pouch of Douglas. The surgeon will wish to remove or obliterate this cul-de-sac. Not only is the peritoneum still sensitive, but also the connective tissue between it and the vaginal epithelium. The injection of a total of 2 or 3 c c of solution into a few of the most dependant parts of the hernia between the peritoneum and epithelium, anaesthetizes a wide area of peritoneum in addition to the pouch of Douglas.

It may be noted here, that if it is desired to remove the uterus the only area requiring additional injection with anaesthetic is that when it is proposed to divide the ovarian nervous plexus, the infundibulo-pelvic ligament if the ovary is to be removed or the upper part of the broad ligament if the ovary is to be retained. If there is still tenderness in the base of the broad ligament, the reason is that the para-cervical injections have not reached as high as the cervical internal os.

It is not suggested that genital prolapse is ever an indication for removal of the uterus. Fothergill's operation cannot be performed unless the uterus is present, and total hysterectomy may make the cure of the prolapse more difficult.

When the patient suffers from urinary stress incontinence, or there is present a so-called urethrocele, the plastic operation must be extended widely on each side of the urethral orifice, in order to repair the sub-pubic fascia. It will be found that anaesthesia in this area is not perfect, and 2 or 3 c c of Novocaine will have to be injected here.

If, in addition to the genital prolapse,

there is also a complete perineal tear requiring repair, it will be necessary to anaesthetize the small area of peri-anal skin that is to be united in front of the bowel, and wise to obtain relaxation of the external anal sphincter by injection of the anaesthetic into the substance of this muscle

Operations limited to the cervix, or to the cervix and uterus, may be completed without pudendal or perineal anaesthesia, provided that the lumen of the vagina is large enough, and the muscles sufficiently relaxed, to allow access to the cervix

Operations limited to the vagina may be performed by the technique of paracervical injection described above, or, if preferred, it is sufficient to infiltrate the subepithelial tissue beneath the vaginal skin

The question of premedication of patients about to undergo operation is debatable. Some surgeons hold that co-operation by the patient is a necessity, that the patient should be capable of refraining voluntarily from movements which may interfere with the ease of operation, and therefore that any premedication which aims at more than calming the patient's nervousness is definitely bad. Unfortunately, many women object to the lithotomy position on account of the mental distress, and also on account of the physical discomfort of the position when the operation lasts longer than half an hour

For these reasons it was considered necessary, when this work was still somewhat experimental, to give all patients some form of pre-operative sedative treatment. Of all the many drugs which have been tried, morphine, together with scopolamine, has given the best results. As is well known, "Twilight Sleep" is, unfortunately, very variable in practice, and it has been found, as experience has increased, that the premedication is of little or no advantage

before minor operations, and it is being discontinued. Before major operations, however, it is still considered necessary, and morphia, gr $\frac{1}{4}$, with scopolamine, gr $\frac{1}{100}$ is given 2 hours before the patient leaves her bed, and the scopolamine is repeated in half the dose 90 minutes later. It is a mistake not to allow the morphia plenty of time to produce its maximal effect

CONTRA-INDICATIONS

The contra-indications to the use of local anaesthesia may be classified under three headings. 1 Acute inflammation—this is rare in gynaecological practice, but a typical example is an acute or subacute Bartholinitis. 2 Anatomical obstruction to the site of injection—the narrow senile vagina of the elderly spinster may prevent access to the vaginal fornices. Also, it has been found difficult, and sometimes impossible, to anaesthetize the cervix of the acutely anteфлекed uterus (the cochleate uterus). Such a uterus is always nulliparous, and frequently associated with a narrow vagina. The acute flexion begins well below the internal os of the cervix, and it is this fact, together with the narrow vagina, which makes it impossible to inject the paracervical tissue exactly where desired. 3 Pathological obstruction to the site of injection—a cervical carcinoma that has spread outwards into the vaginal fornices, offers a barrier that should not be pierced

With the exception of those exhibiting one or other of the above contra-indications, a small and almost negligible list, it may be said that any vulval or vaginal operation may be completed with success under local anaesthesia with one exception, namely, excision of the vulva. It has been found that excision of tissue down to the fascia covering the pubes and deep to the clitoris is painful, and success is not claimed

There are very few indications for vaginal hysterectomy. To quote a surgeon of a previous generation, Howard Kelly (*Gynaecology*, 1928) states that this operation still claims a place in exceptional circumstances, "certain extreme forms of prolapse," and "cancer of the body of the uterus in the aged and feeble, or in diabetics with a fairly lax vaginal outlet." Many will not agree even with these conservative indications. For the purposes of the present subject, the operation has been undertaken 4 times on cases of genital proclivencia in order to demonstrate its possibility under local anaesthesia.

Local anaesthesia will not be found to be an aid to diagnosis in doubtful cases. Abdominal rigidity, especially when associated with excessive fat together with hyperaesthesia of the pelvic organs on palpation, may make a complete diagnosis of the condition of these organs impossible. A general anaesthetic in such a case is a necessity.

It has been stated at the beginning of this article that there are a few simple rules that must be obeyed. 1. Every effort must be made to ensure a comfortable position of the patient on the table. Extreme flexion of the knee joints, owing to the upright leg supports being too short, is the most frequent error. 2. Injection of the fluid must be slow. A rapid increase in tension in any tissue except the loosest, is painful. 3. While the injection is being made, especially if made deeply into a vascular area such as the base of the broad ligament, the point of the needle must be kept constantly moving in order to avoid injection direct into the blood stream. 4. Gentleness is the rule of all surgery, and the surgeon who does not observe this rule would be wise to avoid local anaesthesia. The only exception to the rule of gentleness is in dilatation of the cervix, when sometimes almost brutal force is necessary. There

are limits to this, however, if it is desired rapidly to remove an ovum of greater maturity than 12 weeks, the cervix should be incised as in vaginal Caesarean section. If the pregnancy has advanced further than 5 months and the cervix is closed, it is wise to choose either another route or another anaesthetic.

ADVANTAGES

The advantages of local anaesthesia are quite definite and beyond argument and begin even before the patient reaches the theatre. Instead of the pre-anaesthetic starvation and emptiness so often required by the conservative surgeon, a light meal is given 2 hours before the patient leaves her ward, synchronizing with the first injection of morphia.

During the actual operation it is an astonishing phenomenon that there is very little haemorrhage from cervix, vagina, or the vascular para-urethral area. To watch a vaginal plastic operation performed under general anaesthesia, brings to mind Macbeth's words

'I am in blood

Stept in so far that should I wade no more,
Returning were as tedious as go o'er

Partly as a result of this negligible loss of blood, the general condition of the patient on her return to bed is almost normal. Although vomiting following morphia occurs in about 40 per cent of cases, yet when it does occur it is less severe and of shorter duration than after a general anaesthetic. The patient should, in fact, sit up within a couple of hours' time, and have a light meal of tea and toast and butter. One other advantage may be mentioned, a great blessing to the nursing staff depleted and overworked in war time, the patient does not require practically any special or expert attention during the hours following operation.

The value of local anaesthesia is increased still further if the patient is suffering from one of the ailments, such as respiratory or cardio-vascular disease, that would certainly be aggravated by other types of anaesthetic. Chronic bronchitis, so frequently associated with genital prolapse and especially with stress incontinence of urine, is almost a contra-indication to inhalation anaesthesia.

RESULTS

It has been found impossible by questioning patients during convalescence, to estimate and classify results in degrees of success or failure. Premedication with morphia and scopolamine has two aims: the first, a peaceful sleep while the woman is in the operating theatre, and the second, a state of amnesia for recent events if the sleep is disturbed by unpleasant stimuli. It is well known that both these conditions are not achieved in all cases under twilight sleep. There is an uncertainty about the results of these drugs, and the most frequent cause of failure is the noise and general disturbance of a hospital ward on a busy operating day, so that it is found that both aims are more likely to be achieved when the patient occupies a single room and can be left undisturbed for the 90 minutes before she leaves her bed.

An occasional woman reaches the theatre in a state of mental excitement and hyperaesthesia, and objects strongly even to the touch of a swab on the perineum. Such a patient will protest more strongly still when the first needle enters the perineal skin. In addition to magnifying these unpleasant sensations, she mentally transfers them into painful impressions which she thinks she has received during the operation. The most disappointing comments made by patients were all of the same type, demonstrating this difficulty in assessing success or failure. A woman on whom a Fother-

gill's operation had been performed, told her nurse that she had felt all the stitches, "all four of them."

It is true that when complete amnesia is attained, it may give a false impression of success by masking the failure of the anaesthetic.

Although I have used this technique for every vulval and vaginal operation that is included in my practice of gynaecology, only once has it been necessary to administer a general anaesthetic, this was to a woman who arrived in the operating theatre in a state of such wild excitement that it was impossible to place her in the lithotomy position. No other patient has received even the most minute quantity of general anaesthetic.

The disadvantages associated with this local anaesthesia are few in number. The time occupied in administering the anaesthetic delays the start of the operation for a few minutes, rarely more than 10. The time lost at the beginning is compensated by the negligible amount of haemorrhage during operation. This compensation is, of course, absent in the minor cases.

The patient herself may be upset at the thought of being conscious during the operation, and may ask "to be put to sleep" during the event. It is wise not to inform the patient beforehand of the surgeon's intention. If she herself raises the question, she may be soothed somewhat by the promise that she shall come to the theatre without having to remove her dentures. This proposition is very attractive to some.

On the other hand, the only patients on whom I have had to operate twice under local anaesthesia, have faced the second visit to the theatre without nervousness. All these were women for radium treatment, except one. She was a young, recently married girl, on whom I performed Fall's two-stage operation (*Amer Journ Obstet*

and *Gynecol*, November 1940) for complete absence of the vagina

For many years I have used nothing but soap to clean up the field of operation, and, in order to avoid slippery gloves and instruments, the soap has been removed with surgical spirit. Before the anaesthetic is injected it is necessary to be careful that the spirit does not come in contact with sensitive tissues, especially the urethral mucous membrane.

The bibliography that concludes this article is unusually short, for British literature appears to be silent on this subject, and references to continental journals have not been followed up owing to the difficulty in having these accurately translated at the present time. A large number of articles in American journals has been perused, but little help has been received from them. These few references are of interest, as they show that local anaesthesia in vaginal surgery has been practised in America for over 30 years with success, and that there exists a confusing variation in technique, sometimes depending on a strange conception of the anatomy of the nerves of the pelvis. It may be asked how an operation such as vaginal hysterectomy, requiring infiltration of the parametrium for its success in Missouri, can be performed with equal success in New York under perineal-pudendal block anaesthesia. A partial explanation is offered by the relative insensibility, already noted, of the vagina and cervix.

The present article offers a simple technique based on exact anatomical facts, which will succeed even without premedication.

REFERENCES

Hertzler (Local Anaesthesia, sixth edition) advises injections into the substance of the cervix before operations on this organ. For anterior and posterior colporrhaphy he practises infiltration beneath the epithelium of both vaginal walls anteriorly by multiple injections.

Gellhorn (*Journ Amer Med Assoc* 1913 1354) adopts the technique of Hertzler for operations on the cervix, injecting small quantities of anaesthetic around the periphery and into the broad ligaments, and also into the substance of the cervix at the four points of the compass.

The same author in an excellent article (*Surg Gynecol and Obstet* 1927 105) advises paracervical injections to a depth of 1 inch for curettage operations on the cervix, and vaginal hysterectomy. "Anterior colporrhaphies require injections into the layer between vagina and bladder." "Perineorrhaphies require copious infiltrations." "The tissues between vagina and rectum are infiltrated well beyond the extent of the proposed denudation."

Again (*Surg Gynecol and Obstet* 1930 484) he elaborates his technique for vaginal hysterectomy. Parametric infiltration is now carried to a depth of 1½ inches from the vaginal fornices. The anaesthetic solution is reduced in strength but increased in quantity, and the period of waiting for anaesthesia to supervene is 5 minutes.

Griffin and Benson (*Amer Journ Obstet and Gynecol* November 1941) claim that injection of the pudendal nerve, the perineal branches of the posterior cutaneous femoris, and the perineal fibres of the ilio-inguinal nerve anaesthetise the vaginal mucosa in five minutes. "Also that 'any type of gynecologic vaginal operation can be carried out under perineal pudendal block local anaesthesia.' Among other operations listed are: 'Vaginal hysterectomy, one case. 'Repair hernia cul de sac of Douglas one case'."

REPORTS ON HOSPITALS AND DEPARTMENTS OF PUBLIC HEALTH

THE number of hospital reports received during the past year has shown a regrettable decline. It is only to be expected, however, that the numbers would undergo considerable reduction as the war continues. The chief factors operating against their continued production are reduction of staff and the dissociation of antenatal supervision from lying-in facilities consequent upon the government evacuation scheme. Additional factors are restriction of supplies and the unhappy choice of targets by the Luftwaffe, whereby grievous loss of life has occurred, and many valuable records lost for ever. It is our fervent hope that in the post-war era determined attempts will be made to remedy this defect and we look forward to the reappearance of many familiar annual reports which are now in absentia. The plea oft repeated of previous reviewers for standardization of these reports may be made with more insistence and perhaps with more likelihood of success in happier times.

MIDWIFERY IN THE NORTH-EAST OF SCOTLAND WITH SPECIAL REFERENCE TO THE YEARS 1938, 1939, AND 1940

By DUGALD BAIRD M.D., F.R.C.O.G.

THE report is an analysis of the births taking place in the City and County of Aberdeen during the years 1938-1940. Part I gives a description of the present conditions and a summary of the medical facts with suggestions about improvements which might be carried out. It should be read by the lay public, especially members of local authorities. Part II gives the medical aspect in some detail and should be of interest to general practitioners. Part III deals more particularly with the work of the Maternity Hospital and follows the lines of the annual medical reports published by such hospitals and is therefore of particular interest to obstetricians.

PART I—The Maternity Services (Scotland) Act 1937, makes available to every expectant mother who desires it, the services of a general practitioner and a midwife, and represents a great advance. Provision is also made for specialist and hospital services where required. A scheme based on this Act has been working in the County of Aberdeen for 2 years and has commenced to function in the City of Aberdeen since November 1941. It is generally believed that a midwifery service should be organized on a regional basis round a central maternity hospital and that this hospital should be in close association with a general hospital. The main functions of a central hospital should be (1) The care of women who decide to have their babies in hospital, (2) to maintain a staff of experts to deal with abnormal and difficult cases, (3) to provide undergraduate and postgraduate instruction for medical students and doctors respectively and for the training of midwives, (4) to provide facilities for research work in order that the preceding three functions could be more adequately fulfilled. In the area of Scotland under consideration, the central hospital is represented by a new and first-class maternity hospital at Forrester Hill in close proximity to the Aberdeen Royal Infirmary and Sick Children's Hospital of the University Medical School. An account is given of the available hospital accommodation partly provided by a voluntary body and partly by a local authority. Provision is made for the admission of antenatal cases, and for the isolation of potentially septic emergency cases. The medical and nursing staffs are common to both blocks and it seems that the fullest co-operation exists between the bodies responsible for the administration. A noteworthy feature is the fact that the Registrars are attached to the gynaecological department of the Royal Infirmary and that they are expected to undertake teaching and research work, thus they receive a very comprehensive training. Each of the bodies

responsible for the administration contributes to the salaries of the medical staff, an arrangement which is of benefit to all concerned. Antenatal care of the booked cases is carried out at a central clinic in the town by the staff of the maternity hospital. This staff is responsible for about 300 cases delivered on the district but it is intended that this practice should gradually cease and that the municipal midwives should take over such cases. Pupil midwives and students would still attend such deliveries, and since the medical aid would be the general practitioner booked under the scheme, the latter would have some responsibility for the teaching of students, which would be an incentive to maintain a high standard of work.

A statistical analysis of the maternal, stillbirth and neonatal mortality in the area is given with a view to providing a basis of comparison for the future. The figures quoted show clearly that in the years 1931-35 there was very little fall in the maternal mortality in the City of Aberdeen but a reduction is apparent for 1936-40 and particularly since the opening of the new maternity hospital at Forrester Hill at the beginning of the year 1938. An analysis of the individual causes of death shows that over the whole area the most striking fall in the death-rate has been in deaths from puerperal sepsis; this is attributed to the valuable research work which showed that the haemolytic streptococcus responsible for most of the fatal cases comes directly or indirectly from the upper respiratory tract of someone in attendance at the confinement, and to the beneficial effect of the sulphanilamide group of drugs. An alarming feature is the increase in the number of deaths from septic abortion and a bold policy is advocated suggesting a modification of the law to allow termination of pregnancy in individual cases in which frequent childbearing has combined with overwork and poor nutrition to make the present pregnancy hazardous. A plea for the greater use of blood transfusion is made. An analysis of still birth and neonatal mortality shows that the loss of infant life in the early stages of pregnancy and in childbirth in the City of Aberdeen reaches the very high figure of 72 per 1,000. A detailed analysis of the causes of stillbirth and infant deaths is given with a view to seeing how this figure can be lowered. It is concluded that the mortality among mothers and infants in childbirth in the

Aberdeen area is much too high, and although there are many factors contributing to this unsatisfactory state of affairs it is hoped that the improved nursing and medical services offered in the Maternity Services (Scotland) Act, 1937, if utilized on a wide scale will do much to reduce this mortality.

Detailed Summary PART II.—In Part II deaths occurring in the County and City of Aberdeen during the years 1931-40 have been studied to determine the trend of maternal mortality in the area. The two 5-year periods, 1931 to 1935, and 1936 to 1940 are compared and there is an appreciable fall from 6.3 to 4.1 per 1,000 in the second period. A further sub-division is made the first from 1931 to 1937, and the second from 1938 to 1940, the latter period commencing at the time of the opening of the new maternity hospital at Forrester Hill. In the first period the maternal mortality is 11 per 1,000 and in the second 5.2 per 1,000, a remarkable reduction of 50 per cent the reduction being almost entirely due to the fall in the mortality of book cases.

Further analysis shows that the fall of the death-rate is due to the fall in all categories particularly sepsis. It is noted that although the hospital figures are good they are no better than the figures of certain London hospitals before the discovery of the sulphanilamides. A comparison of the results of domiciliary midwifery in the area under consideration, and that of a working class area in London shows that there is little justification for tolerating the present figure for the City and County of Aberdeen namely that of 4 per 1,000. The English and Scottish figures are not strictly comparable, because in England deaths from intercurrent disease are not included in the maternal mortality figures although they are usually stated in a separate column.

There follows an interesting analysis of the fatal cases in order to assess whether any of them were avoidable. This could only be made with accuracy when the patients died in hospital where full notes were available and where postmortem examinations could be made. The conclusion arrived at was that 18 of the 23 deaths studied were avoidable: inadequate antenatal care; failure to follow medical advice given; and on occasion errors of omission or commission on the part of the midwife or doctor responsible. In the fatal

cases of eclampsia the antenatal care was either poor or none existent

A general analysis of all the fatal cases in the area during the 10-year period, 1931 to 1940 demonstrates that the chief causes of death are sepsis, 35 per cent, intercurrent disease 24 per cent, toxæmia, 17 per cent, hæmorrhage, 12.5 per cent, shock, 9 per cent (The percentages are approximate. Detailed study shows that a striking fall in the number of deaths from sepsis has occurred in the last 2 or 3 years particularly in deaths from hæmolytic streptococcal infection. The introduction of the sulphanilamides is probably the biggest individual factor but other factors including improved hospital facilities have undoubtedly contributed. Pneumonia is the commonest cause of death from intercurrent disease and following the introduction of sulphapyridine the number of deaths from this cause has been greatly reduced. Cardiac disease still takes its toll of pregnant women and there is room for improvement not only as a result of improved care of the cardiac patient when pregnant, but also by advising against pregnancy in women with severe heart disease.

In deaths from toxæmia, inadequate antenatal care appears to have been an all too common factor.

Deaths from hæmorrhage showed a fall from 23 to 15 in the second 5-year period: this is to be expected in view of the increased facilities for providing blood transfusion. In a consideration of deaths due to accidental hæmorrhage, the statement is made 'that the treatment was obviously bad for example in 2 cases packing of the vagina was carried out.' Surely packing of the vagina if properly carried out can be an invaluable method of treatment in certain cases and is advocated by many authorities. In 9 fatal cases of ectopic pregnancy it is stated that several were too ill to operate upon when admitted. Surely this is a defeatist attitude and anyone who has much experience of dealing with these cases will have been impressed by the almost miraculous recovery after operation particularly when blood transfusion has been started during the operation. It is noteworthy that transfusion was employed only once in 10 fatal cases of post-partum hæmorrhage.

Attention is drawn to the alarming increase in the number of deaths from abortion and a sug-

gestion is made that the law should be modified to allow termination of pregnancy in certain cases in which frequent childbearing has combined with overwork and poor nutrition to make the present pregnancy hazardous. It is further suggested that instruction in the best methods of contraception should be made available at all postnatal clinics. The provision of such facilities would do much to prevent unwanted pregnancies which drive the harassed mother to the desperate remedy of procuring abortion.

Stillbirths and neonatal deaths. Stillbirths have only recently become notifiable in Scotland and comparison with the past or with other countries is therefore difficult. More information is available however about the problem of neonatal mortality. The causes of neonatal death are largely the same as those of stillbirth and from Professor MacNeill's articles in *The Lancet* it will be seen that in this connexion Scotland occupies a very unenviable position as compared to England and other countries.

Comparison has been made of the combined stillbirth and neonatal deaths in private specialist practice in booked hospital practice and in domiciliary practice: the comparative figures being 12 per 1,000, 54.5 per 1,000, and 78.5 per 1,000. The low figure in the first group is probably due to the combination of favourable factors—economic, nursing and medical. In the second group the nursing and medical factors are favourable but economic conditions are unfavourable. In the third group the high figure indicates the need for an all-round improvement in medical and nursing care as well as economic conditions. It is suggested that the dietary deficiency could be remedied by a widespread extension of communal dinners. The expectant mother would thus be assured of one meal daily which would contain all the substances thought to be necessary for the well-being of her child. She would have a much-needed respite from cooking and washing-up, and there would be ample opportunity for practical education in the principles of good nutrition.

PART III is a detailed medical and clinical report of the Aberdeen Maternity Hospital for the years 1938, 1939 and 1940, and follows the usual lines of such reports. 4,053 patients were treated with a total mortality of 6.6 per 1,000. The mortality-rate for the emergency cases (36 per

1,000) compares most favourably with that of the booked cases (1.1 per 1,000). The same unfavourable comparison is seen between the combined stillbirth and neonatal mortality which is 54.3 per 1,000 for booked cases and 42.6 per 1,000 for emergency cases. Antenatal complications are enumerated, but details of their treatment are omitted. A point of interest arises, there were 22 terminations of pregnancy, some with sterilization, the indication being general debility and anaemia. Undoubtedly debility and anaemia constitute therapeutic indications for abortion, but the term is capable of very elastic interpretation. Out of 3,427 booked cases, 71 per cent were considered to be normal. The forceps rate of 1.8 per cent is unusually low. In the section on abnormal cases, difficult labour due to contracted pelvis, posterior position of the occiput, and uterine malfunction are classified together because they often occur in the same patient and sometimes it is impossible to say which is the primary factor in causing the difficulty. It is shown that difficult

labour even in booked cases increases the risk to the child by almost 10 times. The incidence of contracted pelvis is estimated by 2.5 per cent. Caesarean section was apparently performed in 50 cases out of 110, but mention is not made as to whether the operation was elective or following a failed trial labour. Actual pelvic measurements appear to have determined the classifications of the various cases and not cephalo-pelvic disproportion.

There were 69 cases of placenta praevia but little or no mention is made of the methods of treatment adopted.

The incidence of non-toxic accidental haemorrhage seems unusually high, 97 out of 144, again no methods of treatment are given.

There is room for improvement in the presentation of the clinical report, particularly with regard to details of treatment, as only by comparing the end results of various methods can each be assessed individually.

Review of Current Literature

Director FREDERICK ROQUES M A , M D , M Chir (Cantab), F R C S F R C O G

THIS Review contains the lists of contents and abstracts of the more important articles from the journals with which the *Journal of Obstetrics and Gynaecology of the British Empire* exchanges

The Review of Current Literature has kept the readers of the Journal in touch with current literature throughout the world, owing to the war many

journals with which the *Journal of Obstetrics and Gynaecology* previously exchanged are no longer received At the end of the year an Index of all the subjects contained in the articles of the journals reviewed is printed Arrangements are also made to include abstracts of important articles on borderline subjects, such as Physiology Biology, and Biochemistry

LIST OF ABSTRACTORS

J LYLE CAMERON, F R C S
W E CROWTHER, M B
R H B ADAMSON, M D
B JEAFFRESON F R C S

P MALPAS, F R C S
T N A JEFFCOATE F R C S
MEAVE KENNY F R C S
JANE H FILSHILL

The British Medical Journal

September 19th, 1942

*Shortage of practising midwives Annotation

September 26th 1942

*Maternal pulmonary embolism Annotation

October 3rd 1942

Woman power and maternity General Article

October 10th 1942

Tetanus in the puerperium A T Duncan
Maleness, femaleness and mental disease
Annotation

October 17th 1942

*The sterols their structure and action Annotation

October 31st 1942

Unusual case of injury to female urethra R H
Cooke, and D J N Smith

November 7th 1942

*Foetal and postnatal circulation Leading article

SHORTAGE OF PRACTISING MIDWIVES

The number of midwives on the roll in England and Wales is just over 65,000 but only about 24 per cent of these are actually in practice

There is no shortage of pupil midwives but only 58 per cent of women who enrolled as midwives in 1940 were practising in 1941

The Central Midwives Board considers that the permanent solution to this problem can be achieved only by an improvement of pay and conditions of service

MATERNAL PULMONARY EMBOLISM

Steiner and Lushbaugh from a series of 72

maternal deaths investigated in the Department of Pathology of the University of Chicago have opened a new field of thought in sudden maternal deaths They maintain that the most common cause of sudden death during labour, or in the first few hours after delivery is pulmonary embolism due to passage of meconium liquor amni or vernix into the maternal circulation

In the cases quoted there was a fairly constant clinical picture of violent uterine contractions followed by a rigor and then a condition of shock. Vernix and meconium were identified in the smallest pulmonary arteries

Experimental studies on dogs and rabbits showed that death could be produced by the intravenous injection of meconium and amniotic fluid and that the animals die from anaphylactic shock

THE STEROLS THEIR STRUCTURE AND ACTION

The phenanthrene ring is present in narcotics of the morphine group bile acids cholesterol, vitamin D the sterol hormones and many carcinogenic hydrocarbons Selye investigated the modifications of the cholane ring which characterize the sterol subgroup and observed the effect upon six different types of action These are called the folliculoid corticoid luteoid testoid gonadotrophic and anaesthetic

All sterols with a side chain of two or less C atoms have some activity but the long side chain derivatives are inert The folliculoid and anaesthetic activities are the most common and stil-

boestrol also, although not immediately related to the phenanthrene group, has a well-marked anaesthetic action in addition to the well known follicular action

FETAL AND POSTNATAL CIRCULATION

Investigations of the foetal circulation in sheep have been carried out with X-ray cinematography after the injection of radio opaque media into a foetal vein. At the same time the foetus was prevented from breathing in order to disturb the normal intrauterine conditions of life as little as possible.

These experiments have demonstrated the division of the inferior vena caval flow into two streams. The larger of these two streams passes

through the foramen ovale into the left auricle whilst the smaller stream enters the right ventricle through the tricuspid opening.

In addition the flow of the superior vena cava passes entirely through the right auricle and ventricle into the pulmonary trunk and thence via the ductus arteriosus into the descending aorta and pulmonary arteries. Only a small amount of the blood from the placenta is by passed through the ductus venosus—the larger proportion passing through the liver substance.

Some new terms are introduced owing to variations which are met with in different animals rendering inappropriate some terms used in human anatomy.

JOHN HAMMON

The Canadian Medical Association Journal

Vol XLVI February 1942 No 2

*Radium treatment of carcinoma of the cervix
E. Trapp

Vol XLVI, March 1942 No 3

*Surgical and gynaecological experiences with an emulsion of sulphathiazole D. Ackman and G. Wilson

RADIUM TREATMENT OF CARCINOMA OF THE CERVIX

Radiological treatment of cancer of the cervix has afforded one of the most successful chapters in the field of cancer therapy. In the Cancer Commission of the League of Nations set up in 1924, the decision to deal with cancer of the cervix uteri by irradiation in the treatment of this condition was established. A sub-commission of radio therapists and gynaecologists under the chairmanship of Prof. Regaud of Paris was formed, and it was decided to confine the first investigation to three clinics, viz. the Radiological Institutes of Stockholm, of Paris, and the Frauen Klinik of Munich. An international record form was adopted and reports of international procedure and methods of treatment were arranged. In establishing a basis for comparing statistics rules were adopted (1) to define precisely the different varieties of utero vaginal cancer (2) to classify cancer of the cervix according to stages depending upon the anatomical extent of the growth (3) to define data necessary for statistical reports, (4) to compute the results of treatment and (5) to

record data of the technique of treatment. The first report was published at Geneva in 1929. When the health organisations met at Zurich in 1924 it was recommended that an analysis of the results of treatment by radiotherapy in cancer of the cervix estimated after a period of observation of 5 to 7 or more years should be published annually. The first of these reports was issued at Geneva in 1937, and contained records of methods and results from six different clinics and contained the reports of five-year results on 757 patients treated in 1930. The second report published in the following year referred to cases treated in 1931 and previous years. It contained the results of nine different centres and contained records of more than 6,000 patients, of whom 86.3 per cent had been treated radiologically. The third and last report appeared in 1939. It contained records of more than 9,000 patients treated at 16 different centres in 1932 and the previous years. Another important report of work and statistics was that first given by Dr. Janet Lane Clayton in 1926 in her monograph, she collected and classified the final results of treatment by surgery and radiology in 80,000 cases which had been under the care of different clinics. The survival rate was found to be almost the same for both methods of treatment but the surgical methods were only those of operable cases and it was at once apparent that radiotherapy has the advantage of greater applicability. It was this report by Lane Clayton which chiefly influenced the choice of the uterus for the first

clinical research work of the League. Records were also collected all over North America and from other parts of Europe and exhaustive analyses of these have been made. The results of these have shown that radiation treatment of cancer of the cervix had practically the same end results as treatment by surgery, was more widely applicable and was devoid of most of the disadvantages of the latter. The result has been that in certain German clinics, such as Heidelberg and Munich, no cases of cancer of the cervix were submitted to operation after 1913. Sweden gradually adopted the same measures and since 1920 almost all these cases have been treated by radium. British and American clinics have been slower in adopting this attitude. However, in recent years almost all the clinics have accepted radium as the treatment of choice in cancer of the cervix.

Radium is now supplemented by deep X-ray therapy, for radium has a lethal effect on cancer cells only within a radius of 3 cm. Some clinics, however, such as that of Stockholm, employed telerradium therapy in place of X-rays. This latter method has been used in the London Institute and the Chicago Tumour Institute. Ten gramme bombs of radium are being used and the directors are satisfied that with improved technique they may be of greater value than X-rays.

The latest advance in radium treatment of cancer has been an estimation of the amount of irradiation most suitable to steer safely between the dangers of over dosage and under dosage. One of the internationally adopted units is what is known as the Sievert dose, i.e. the amount of gamma irradiation received in one hour at 1 cm from 1 mgm of radium with a filtration of 0.5 mm of platinum. The acceptance of this unit simplified the situation of the physicists to determine the amount of radiation, especially when considered three dimensional measurements. All the researches carried out at numerous clinics in Great Britain, the Continent and the United States have made it a standardization of dosage and application. Two outstanding methods were employed: one known as the Paris method in which continuous radiation at low intensity was given, and the other, the Stockholm technique, employed divided doses at relatively high intensity delivered in two or three applications. All the well established clinics employed one or other

of these methods and neither of them has been shown to have superiority over the other.

The Stockholm method was developed from the work of Forssell, who began treating cancer of the uterus with local application of radium salts in 1910. Only 10 to 20 mgm were used and the time of application was usually limited to 20 hours. In favourable cases the treatment was repeated a number of times at intervals of 3 to 6 weeks. When more radium was available, larger doses were used and immediate improvement was observed with fewer applications. By 1914 the present method was established. By 1936 3,000 cases had been treated and observations over this time showed that the additional factor which had materially improved the percentage of cures was the use of deep X-ray radiation or telerradium therapy, in combination with the local application of radium. One important principle was always maintained, viz. the adaptation of the technique to the local conditions prevailing. This entailed a supply of radium in various forms and sizes of containers.

The author's technique is reviewed. A general and a local examination are made. When much infection is present or if the cancer has progressed to stage 3 or 4, deep X-ray treatment is given prior to radium therapy. When the cervix can be found and dilated a central stem made of different segments containing amounts varying from 10 to 80 mgm is inserted through the cervix into the uterus. Further amounts of radium in London colpostats are applied all round the central stem. These latter alone are used when it is impossible to find the cervical canal, a procedure which is almost invariably possible at the second application. The containers are left in position for 20 to 24 hours. The usual single dose is about 1,000 mgm hours inside the cervix and uterus and 1,500 in the vagina, the total dose being 7,000 to 8,000 mgm hours. The second application is given in one week, and the third two or three weeks later. A white membranous film appears two or three weeks after the first treatment. It tends to subside in about three weeks after the third treatment and to reappear after X-ray radiation. Occasionally there is ulceration becoming secondarily infected following too vigorous treatment. This occurs six months to a year afterwards. It is important to remember this, as the condition may be mistaken for a recurrence, for radiation would only aggra-

vate the condition. Treatment should not be repeated within the first year if a maximal dose has been given. Remnants of growth or small recurrent nodules in the vagina may be implanted with radium needles.

It may be mentioned, in addition, that Heyman has developed a successful method for treatment of carcinoma of the body of the uterus with radium. By his method he completely fills the uterine cavity with radium capsules of equal size, the total dose is given in two treatments with an interval of three weeks, the quantity of radium varying from 80 to 200 mgm. and the total dosage from 2,600 to 4,000 mgm. hours. The patients are kept under observation and if symptoms do not disappear, or if bleeding, discharge or increase of the size of the uterus appear total hysterectomy is performed.

From a consideration of all the facts available it is evident that the best results are obtained in clinics where all treatment is carried out or supervised by one person preferably by a permanent staff and co-ordinated team work and due consideration must always be given to planning the treatment and moulding it to the requirements of each individual case.

SURGICAL AND GYNAECOLOGICAL EXPERIENCES WITH AN EMULSION OF SULPHATHIAZOLE

The usefulness of sulphanilamides in powder form for local and regional treatment is now believed to be established. The employment of these drugs in solution was considered and the authors independently had directed their attention to the use of sulphonamide emulsions. It had been stated by Locatelli and Bowden that sulphanilamide in an ointment base is inert but in liquid paraffin it maintains its full bacteriostatic action. This action appears to be dependent upon the fact that the liquid paraffin covers the wound intimately and prevents the adherence to its surface and coagulation there of lymph thus permitting a constant exudation of fresh leucocytes and antibacterial products. These views led to the choice of a sulphonamide emulsion of oil and water.

In choosing a suitable sulphonamide the following factors were considered viz., the maximal local bacteriostatic action, the minimal toxicity of the absorbed chemical, and finally its commercial availability and cost. Sulphathiazole was the

substance most nearly fulfilling the demands. The concentration of the drug was finally set at 5 per cent as the result of the work of Winer and Strakosh, who showed that this percentage produced the maximal effects. The following emulsion was evolved—sulphathiazole finely powdered 5 per cent, triethanolamine, 2 per cent distilled water 24 per cent white beeswax 5 per cent, and liquid paraffin, 64 per cent. This preparation is believed to promote drainage to be applicable to all wounds, and to be attended with a minimal risk of toxicity from absorption.

In gynaecological practice gauze soaked in this emulsion forms a most excellent pack for the vagina, in that it promotes free drainage, permits firm packing of the vagina to diminish oozing of blood, and has a very powerful bacteriostatic action. It is very useful here as the vagina is extremely difficult to sterilize.

The sulphathiazole emulsion is applied in a two inch wide gauze strip and packed into the vagina. This may be employed before operation and is useful when decubitus ulcers are present on the prolapsed cervix or vagina and when there is evidence of senile vaginitis. This pack need not be disturbed for a period lasting from 48 to 72 hours. The authors followed this line of treatment in 83 consecutive cases, with the result that there were fewer cases of sepsis, diminished dehydration of the vagina and a freedom from decomposition with resultant foetor when the pack was removed. There was marked freedom from symptoms indicating absorption of the drug, which was only found in a very small trace when assays of the blood were made.

One important point must be stressed: the vagina should be free from alcohol before it is packed with sulphathiazole otherwise local necrosis may result. The use of sulphathiazole emulsion was further extended. It was freely used when packing for haemorrhage attending incomplete abortion was necessary. It was also used successfully when suturing a complete perineal tear a result which led the authors to suggest that sulphathiazole emulsion gauze might be of considerable value in packing the rectum after the removal of haemorrhoids.

A considerable bibliography and an excellent resume in French by Jean Saucier are appended.

J. LYLE CAMERON

THE
Journal of Obstetrics & Gynaecology
of the British Empire

VOL 50, No 4

NEW SERIES

AUGUST, 1943

Phases of Maturation, Fertilization and
Early Development in Man

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INTRODUCTION

AN account is given by Allen and others¹ of attempts that have been made in the past to secure human tubal ova. They recovered 5 ova by reverse irrigation of the uterine tubes from the uterus. An unfertilized ovum was recovered by Lewis² by flushing the uterine tube which had been previously removed with a myomatous uterus, two other ova were recovered by Pincus and Saunders.³ Rock and Hertig⁴ report the recovery of an unfertilized ovum, but do not give any details concerning it.

Until the publication by Dible and West,⁵ and that by Hertig and Rock,⁶ and more recently the account of young embryos given by Rock and Hertig,⁴ the youngest human embryo was the "Miller" described by Miller⁷ and Streeter⁸, unfortunately only 5 sections were preserved.

The present communication gives a description of an unfertilized ovum showing

the second maturation spindle, an unsegmented ovum at an early stage of fertilization, and a young chorionic vesicle partially implanted in the endometrium.

DESCRIPTION

The first specimen was obtained from a woman who was sterilized on account of severe mitral stenosis. The ovum was recovered by flushing the uterine tube after its removal on the 17th day of the menstrual cycle, ovulation probably occurred less than 12 hours before. The cycle previous to that from which the ovum was recovered was of 30 days duration. At the operation the right ovary showed a recently ruptured follicle with a small amount of blood still escaping. When examined in the fresh state the ovum was surrounded by several layers of corona radiata cells which were attached to a homogenous zona pellucida (Plate I,

fig 1) The vitellus was yellowish in colour, uniformly finely granular and completely filled the zonal cavity. It did not show the three types of yolk bodies described by Lewis,² but resembled more closely the second ovum described by Pincus and Saunders.³

After fixation the ovum was found on histological section to be at the stage of the second maturation spindle (Plate I, fig 3). The polar body showed scattered chromosomes in its cytoplasm. Dixon⁴ concluded from an examination of an oocyte in the ovary that the second maturation spindle was completed before the oocyte left the ovary but the appearances found in this specimen and in the descriptions given by Allen and others¹ for two of their shed ova and by Pincus and Saunders³ do not support Dixon's opinion. Whether the second maturation division is completed in the absence of fertilization cannot be stated at present.

The second specimen was obtained from a woman who was sterilized as her last 2 pregnancies terminated as miscarriages on account of severe toxæmia. Her menstrual cycles previously were of the 28 day type. The ovum was recovered by flushing the tube removed on the 16th day of the cycle, coitus had taken place 2 and 4 days previously. At the operation the ovary showed a recently ruptured follicle with some blood still escaping. When examined in the fresh state the ovum was found to be free of corona radiata cells. The zona pellucida appeared as a homogeneous membrane in which many completed sperms were found (Plate I, fig 4). The vitellus did not completely fill the zonal cavity, at one side there were a number of granules, probably remains of the polar bodies. The vitellus showed a clearer zone in the centre and its general appearance was that of early degeneration.

The third specimen (the "Barnes" embryo), an early chorionic vesicle partially implanted in the endometrium, was found after hysterectomy on the 25th day of the menstrual cycle. The patient had an ovarian cyst and was suffering from excessive menstrual loss. Coitus had taken place on the 10th and 12th days previous to the date of operation.

At the operation a considerable amount of free fluid was found in the peritoneal cavity. The left ovary contained a cyst about 4 inches in diameter and also a corpus luteum. The uterus was slightly enlarged and soft. As the nature of the ovarian cyst was in doubt a total hysterectomy, bilateral salpingectomy, and left oophorectomy was performed. The appendix was also removed.

The uterus was incised along the attachment of the broad ligament on each side and was then opened, separating the anterior and posterior walls from each other. The endometrium in the cervix and in the lower part of the body was hypertrophic and polypoidal. The endometrium lining the remainder of the uterine cavity appeared to be normal, it showed, in approximately the middle of the posterior wall, a small elevation which was just visible to the naked eye. On examination with a low power binocular microscope the elevation appeared as a slightly raised translucent area which was clearly demarcated from the surrounding endometrium. The elevation was tentatively diagnosed as a young implanting blastocyst or a retention cyst of a uterine gland.

After fixation with Bouin-Allen the area became opaque but was still raised above the level of the surrounding endometrium (Plate II, fig 5). A block of the uterine wall containing the swelling was removed and after dehydration, clearing and double embedding was cut at 7μ . Microscopical examination of the sections showed

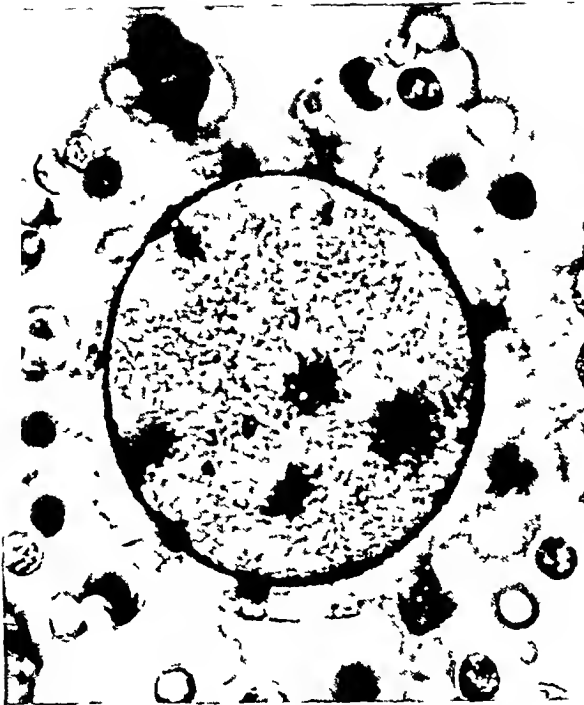


FIG 1 Photomicrograph of ovum No. 1 in the living state. The dark areas on the vitellus are corona radiata cells on the upper or lower surface of the zona. $\times 180$

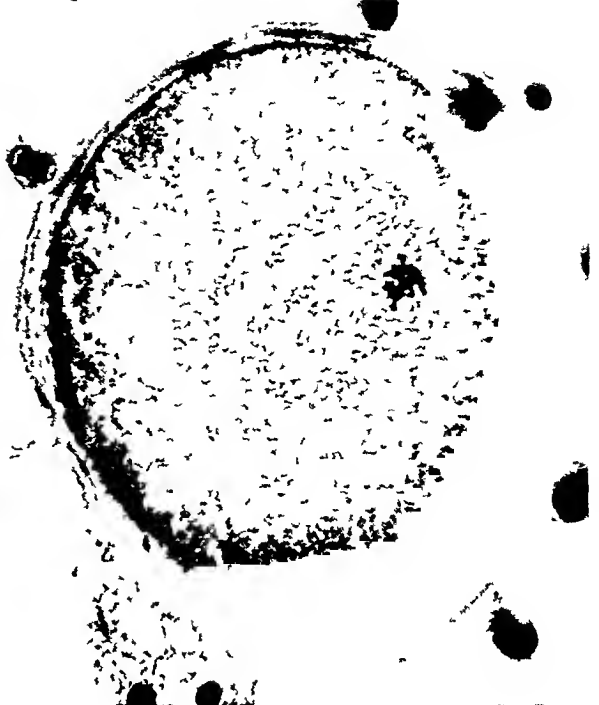


FIG 3 A section of ovum No. 1 showing the metaphase of the second maturation division. The first polar body (out of focus in the upper right-hand corner) is seen. The vitellus has shrunk from the zona pellucida and most of the corona radiata cells have been lost (cf Pl I Fig 1). $\times 820$



FIG 2 The same ovum immediately after fixation. $\times 480$

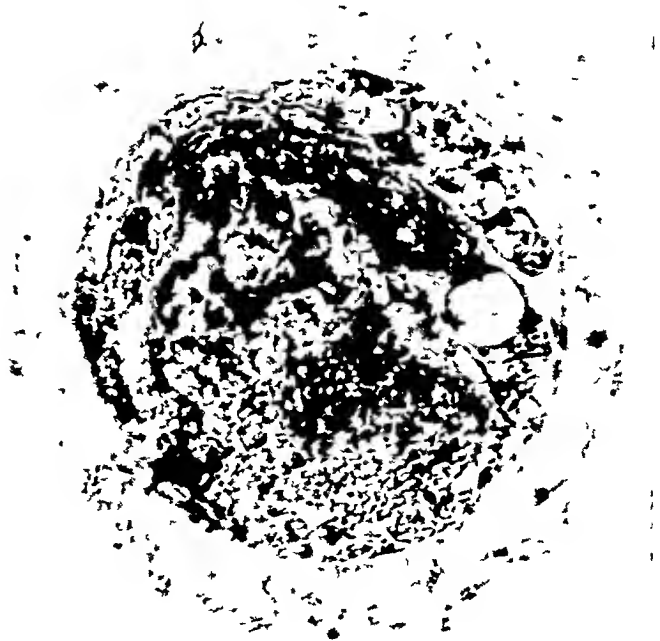


FIG 4 Photomicrograph of ovum No. 2. A complete sperm is seen in the zona pellucida; other sperm heads are visible. At the upper right hand corner of the photograph globular detritus is seen. $\times 480$

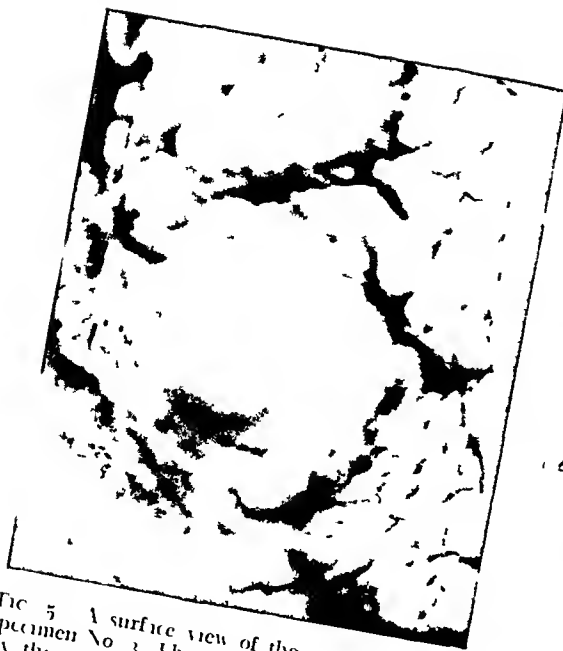


FIG 5 A surface view of the endometrium of specimen No. 3. The smooth elevation produced by the implanting embryo is seen. The endometrium shows fissures and crevices which for the most part are associated with the mouths of the uterine glands. $\times 17$



FIG 6 A high power view of the embryonic disc showing the columnar nature of the embryonic ectoderm and the arrangement of the endoderm with Heuser's membrane. The cells of the latter are continuous. $\times 400$



FIG 7 A general low power view of the implanting embryo and surrounding endometrium. The latter is oedematous and in it there are many dilated blood vessels. The extent of the syncytiotrophoblast and cytotrophoblast in different parts of the vesicle is shown. The extra-embryonic mesoderm has been artificially separated from the cytotrophoblast except at the embryonic pole. The embryonic rudiment has differentiated into a columnar ectoderm and liver which at the edge of the embryonic disc is continuous with the embryonic ectoderm of the inner Heuser's membrane enclose a cavity the primitive yolk sac. $\times 110$

an early implanted blastocyst (Plate II, fig 7) The chorionic vesicle is not completely implanted in the endometrium as part of the elevation that projects into the uterine lumen is not yet covered by the uterine epithelium This relatively superficial position of the chorionic vesicle in the present specimen resembles closely that of "ovum" No 7700 of Hertig and Rock⁶ The trophoblastic shell varies in thickness, it is thickest over the deep embryonic region of the vesicle and thinnest in the abembryonic region where the uterine epithelium is absent The trophoblast is differentiated into a cytotrophoblast and a syncytiotrophoblast The calculated dimensions of the vesicle are approximately $0.931 \times 0.770 \times 0.737$ mm In some areas the syncytiotrophoblast has destroyed the wall of the blood vessels, allowing the blood to escape to a slight extent into the intercommunicating lacunae of the syncytiotrophoblast The general appearance resembles very closely those described and illustrated by Hertig and Rock⁶ The peripheral edge of the syncytiotrophoblast, however, seems to be more sharply demarcated from the endometrium than in their specimens Nos 7699 and 7700 and resembles more closely the appearance in their specimen No Re 7950, Fig 4 (1942) The cytotrophoblast is composed of cuboidal cells which in some situations have proliferated to form irregular masses which project into the syncytiotrophoblast, these projections are the forerunners of the primary villi

The endometrial tissue shows marked oedema, but there is no evidence of a decidual reaction The glands of the endometrium are dilated and tortuous Their epithelium seems to be resistant, at this stage, to the action of the syncytiotrophoblast and the glands appear to be pressed aside by the expanding vesicle (cf Streeter, 1926)

The embryonic disc is convex towards the amniotic cavity and is composed of tall columnar epithelial cells which are continuous at the periphery of the disc with the amniotic ectoderm (Plate II, fig 6) This for the most part consists of a layer of flattened cells but in one situation these cells are cuboidal The endoderm is composed of from one to several layers of large cuboidal cells with vacuoles in their cytoplasm In the younger embryo No 7699 described by Hertig and Rock the endodermal cells are heaped up to form a mass as many as three layers thick but in their other specimens the endoderm forms a single layer An endodermal yolk sac has not yet been formed but a cavity lined with endodermal cells and flattened mesodermal cells (Heuser's, or exocoelomic, membrane) encloses a cavity (Fig 7) which has been designated by Hertig and Rock⁶ in their specimens as the exocoelomic space In this cavity there is a precipitated coagulum The outer aspect of the cells of Heuser's membrane is continuous with a mesenchymal reticulum which fills the trophoblastic vesicle except where it has become artificially separated from the cytotrophoblast

Probable age of the specimen

As already stated cortis occurred 12 and 10 days before the operation The last menstrual period began on the 25th May and, assuming that the present cycle would have been of 28 days duration, the next period was due on the 22nd June Cortis occurred on the 6th and 8th June, i.e., 16 and 14 days before the expected next period The operation was performed on the 18th June If ovulation occurs (see later) 14 ± 1 (i.e. 13 to 15) days before the next menstrual period then ovulation occurred on the 7th to 9th June A comparison of the present specimen with those of Hertig and Rock shows that No. W1

8004 which is estimated to be $9\frac{1}{2}$ days old, is much less developed. The embryonic disc of No 7699, estimated age 11 days, is less developed but the syncytiotrophoblast has invaded the endometrium more than has that in the present specimen. It seems probable that ovulation occurred at the earliest on the 7th—8th June, and that the fruitful coitus was that of the 6th June. The age of the embryo is thus estimated to be from 10 to 11 days, mean age $10\frac{1}{2}$ days.

TIME OF OVULATION

~ On the time of ovulation in women there is now an extensive literature which has been reviewed by a number of investigators (Knaus,¹⁰ Dickinson,¹¹ Latz and Reiner,¹² and others). The evidence which has been accumulated during the past few years from a number of different methods of investigation seems to show that ovulation is more closely related to the succeeding menstrual period than to the beginning of the preceding menstruation. Ogino¹³ Pryde,¹⁴ Smith,¹⁵ and Latz and Reiner¹² base this assumption on their investigations on the so-called "safe period." Schroeder¹⁶ and Shaw¹⁷ deduce the time of ovulation from the examination of the endometrium and related corpora lutea, and conclude that it occurs at about the middle of the cycle. Rock and Hertig,¹ by comparing the ages of young embryos with the associated endometrial histology, conclude that ovulation occurs 13 to 15 days before the next menstruation.

It is thus presumed that ovulation occurs about 14 ± 1 days before the beginning of the next menstrual period. The day, however, cannot always be accurately predicted since there is some variation in the length of the menstrual cycle in individual women. Gunn and others¹⁸ state that no cases were found which did not vary at least 2-75 days between the shortest and

longest interval, and Haman¹⁹ states that there was no instance of absolute regularity in his series. Further, Rock²⁰ has suggested that about 3 per cent of the women in his series of 88 cases do not ovulate regularly 13 to 15 days before the next menstrual period and, therefore, do not fit into the general pattern.

The recovery of ova at a definite period of the menstrual cycle gives the most reliable information on the time of ovulation. Specimen No 1 of the present series which was presumed to be recently shed since it was surrounded by many corona radiata cells was recovered 14 days before the presumed beginning of the next menstrual cycle. Table I gives the estimated age of all ova described up to the present and the approximate day of their recovery in the cycle. There is some evidence from these few cases to show that the time of ovulation is more closely related to the beginning of the next menstruation than of the preceding one.

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TABLE I

Ovum	Corona cells	Polar bodies	Day of cycle ovum recovered	Length of menstrual cycle	Presumed number of days between ovulation and onset of next cycle	Remarks
Allen and others						
1	Nil	2 (19a)	15th	Not stated	—	Ovum lost
2	Present	1	15th	Not stated	—	Twins—one from each ovary
3	Partly dispersed	1	15th	Not stated	—	
4	Partly dispersed	1	16th	Not stated	—	
5	3 layers	—	14th	Not stated	—	
Lewis	Nil	—	22nd	Formerly 28 days, last 35	14-15	Ovum possibly 1 day old
Pincus and Saunders						
1	Nil	—	19th	28 days	12	Ovum possibly 2 days old
2	Nil	1	20th	26-30 days	9-13	Ovum possibly 2 days old
Present paper						
1	Present	1	17th	Formerly 28 days, last 30	14	Not more than 12 hours old
2	Nil	2 Polar debris	16th	28 days	14-15	Ovum lost, possibly 1-2 days old

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Two Cases of Renal Failure Following Abortion

BY

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THE two cases here described occurred within 3 months of each other in the Redhill County Hospital, Surrey. The first patient was a woman of 31, who was known to have had some degree of toxæmia in her previous pregnancies and to have had a residual hypertension, her illness had a fatal termination. The second patient was a girl of 18 years, in her first pregnancy. She gave a history of a fall and symptoms suggested a concealed accidental haemorrhage. After a long illness she has been discharged convalescent.

CASE I

Mrs D., aged 31. Married 3 children (1931-1933-1936).

Previous history. No scarlet fever, no tonsillitis. Had been attended by her doctor in each of the previous confinements for "kidney trouble". In the last confinement there was marked albuminuria, and raised blood-pressure. Some months later the blood pressure was 160/100. When seen by her doctor in February 1942, she was 6 months pregnant and showed symptoms of severe toxæmia. She was given a note advising admission to hospital, but she delayed coming to hospital for 5 days.

Condition on admission. February 10th 1942.

Complained of headache, misty vision and spots before her eyes. Chest nil. Heart apex-beat $4\frac{1}{2}$ inches out from mid-line, tachycardia. Abdomen uterus the size of a 24 to 26 weeks pregnancy. Very slight pre-tibial oedema. Small retinal haemorrhages. Marked albuminuria. Blood-pressure 230/155.

Morphia gr $\frac{1}{4}$ given, also 10 c.c. of 10 per cent magnesium sulphate given intravenously on admission.

February 11th, 1942. Refused to have induction of labour.

February 12th, 1942. Patient worse. Complained of inability to see, also of pain in the chest. Heart enlarged $4\frac{1}{2}$ inches to the 6th interspace. Triple rhythm. Tachycardia. Marked dyspnoea. Fine crepitations at bases of both lungs. Petechial rash and haemorrhages on legs and abdomen.

5.30 p.m. Artificial rupture of membranes after catheterization. Ten ounces of dark-brownish urine withdrawn. Blood was not confirmed.

10.20 p.m. Delivery of foetus (26 weeks).

February 13th 1942. 2.50 a.m. Completion of 3rd stage of labour. During the day $\frac{1}{4}$ ounce of urine was secreted. Blood pressure dropped to 100/85.

Intravenous drip commenced—10 per cent of glucose in distilled water with 2 per cent soda bicarbonate (2 ounces four-hourly). The drip was kept going more or less continuously for several days in the hope of encouraging the kidneys to work until oedema became marked. The blood pressure rose gradually as did also the blood urea. Magnesium sulphate was introduced into the duodenum by means of a Ryle's tube when the patient was unable to take it by the mouth—together with enemas, was to encourage the elimination of fluid by the bowel. Linseed packs were applied to the kidney area. Heart stimulants were given but the patient became gradually more oedematous, more irrational, finally comatose and died on the 8th day after delivery.

The course of the illness, the change of blood pressure, urine urea, blood urea, also the output of fluid are shown on the accompanying chart.

Post-mortem findings

Heart. Left ventricle hypertrophied but not dilated. Valves normal.

Liver. Serous surface smooth. Cut surface appeared normal.

CASE 1

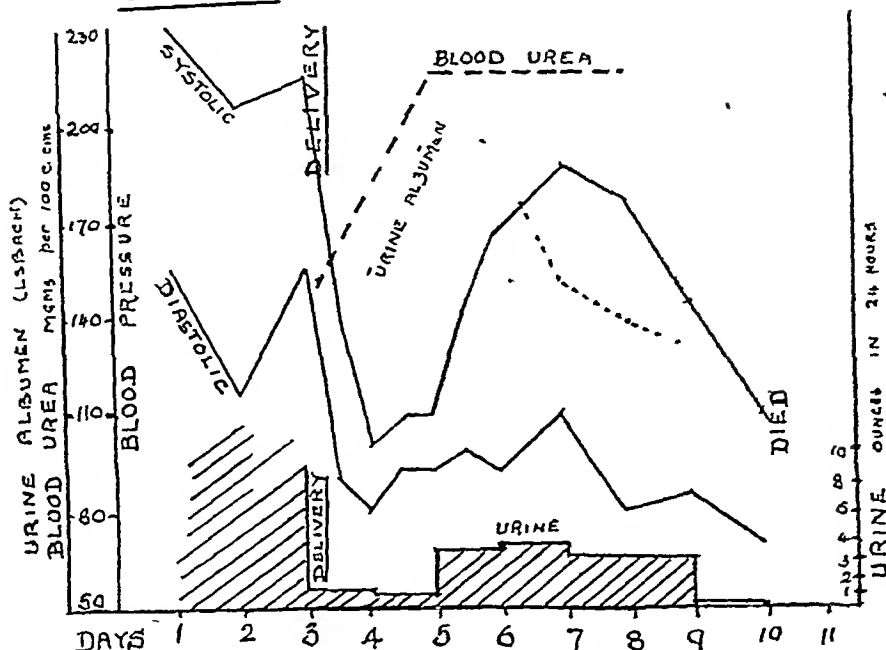


Chart showing blood-pressure, blood-urea output of urine and urine albumin (Esbach)

Spleen Hard—some fibrotic areas
 Blood vessels No atheroma or sclerosis
 Kidneys Large—subcapsular haemorrhages
 Capsule peeled well

Cut surface Both kidneys showed complete bilateral cortical necrosis—very little normal substance seen The whole of the cortex was greyish-white, with haemorrhages along the inner edge There was a thin layer of more normal looking substance just under the capsule

Ureters Slightly dilated

Uterus Endometrium brownish and ragged
 Placental site showed evidences of infection

Section of kidney

Section showed subacute nephritis, without evidence of chronic nephritis

Family history Father died of pulmonary tuberculosis

Previous illnesses Rheumatism and chorea at 4 years of age Scarlet fever at 8 years—in bed 14 weeks Pleurisy at 16 years Pleurodynia 8 months ago

History of present condition

May 14th 1942 Fell down five steps and split her legs Took train home (8 miles) No discomfort that night

May 15th 1942 Attack of giddiness with back-ache when out in the morning Walked home with help and found that she had a small loss of blood Doctor sent her into hospital

Condition on admission

Temperature 97.2°F Pulse-rate 100 Respiration-rate 20 General condition good Blood-pressure 95/68

Uterus Size of 26 weeks pregnancy Marked contractions Foetal heart not heard Vertex presentation

P V Cervix taken up—os not dilated

May 16th 1942 Aborted at 3 a.m. Complete 3.40 a.m. Foetus not macerated Weight 2 pounds

CASE 2

Mrs I aged 18 Married Primigravida
 Emergency admission on May 15th, 1942, at 6 p.m.

Complained of vaginal haemorrhage and abdominal pain after a fall on the previous day Pregnancy about 6 months

8 ounces Quiet day Blood-pressure 90/68
8 p m Had not passed urine all day 1 c c Car-
bachol given without result 10 30 p m Patient
catheterized Ten ounces of deeply blood-stained
urine withdrawn

May 17th, 1942 Still not passing urine nor-
mally On Catheterization the urine was deeply
stained with blood Morning specimen appeared
to be almost pure blood later specimens were less
deeply stained Intravenous drip guaco saline
commenced Urinary deposit showed uric acid
crystals epithelial cells an average of 16 pus cells
and 1 red blood corpuscle per field Casts were
not seen Gram negative bacilli and gram positive
cocci were present

May 18th, 1942 Blood-pressure rising Still not
passing urine Urine contained large numbers of
red blood cells and pus cells One blood cast was
seen

May 19th, 1942 Condition fairly good Blood-
pressure 135/75 Linseed poultices to lumbar
region

May 20th 1942 General condition maintained
Urine amphoteric albumin present (Guaiacum
test for blood negative)

May 21st, 1942 Blood-pressure 145/98 Marked
oedema of vulva and ankles Right arm vein
thrombosed Urine alkaline Many-red blood
corpuscles and pus cells albumin present Deposit
showed epithelial cells many red blood corpuscles
and an average of 7 pus cells per field Casts not
seen The culture was sterile Seen by Professor
Young One pint of plasma given Vein throm-
bosed

May 22nd 1942 Condition still fair Blood-
stained alkaline urine albumin present, no sugar,
deposit showed epithelial cells, red blood cor-
puscles and an average of 7 pus cells per field
Culture sterile Temperature rose to 103 F in the
evening

May 23rd 1942 Condition deteriorating—
oedema increasing Vomited frequently during
the day One pint of plasma given, followed by
one pint of blood Swinging temperature up to
103°F at night

May 24th 1942 Condition very grave Right
saphenous vein thrombosed and canula had to be
withdrawn Leg became very swollen and pain-
ful

May 25th 1942 Slight improvement in con-

dition Vulva and back still very oedematous
Right leg very painful Temperature swinging
Left saphenous vein thrombosed

May 26th, 1942 Marked diuresis established

May 27th, 1942. Patient very ill Diuresis
maintained Vulva, ankles and back still very
oedematous

Blood Red blood corpuscles, 4 000 000, poly-
morphs, 89 per cent white blood corpuscles
35 400 lymphocytes 9 per cent haemoglobin
80 per cent, eosinophils 1 per cent, colour index
1 large mononuclears, 1 per cent

Patient restless and irrational at night

May 28th, 1942 Diuresis 248 ounces Very rest-
less and irrational Oedema subsiding

May 29th, 1942 Complained of cough and of
sharp stabbing pain in chest on left side

June 1st, 1942 X-ray examination of the
chest left base is dull and shows congestion

June 2nd 1942 Patient not so well Marked
twitching of facial muscles

June 3rd, 1942 General condition slightly
improved

June 6th 1942 Impossible to obtain any
samples of blood, because of immediate clotting of
blood

June 10th, 1942 White cell count 9 400 per
c mm Polymorphs, 62 per cent lymphocytes 37
per cent eosinophils none basophils none, large
mononuclears, 1 per cent

Relative lymphocytosis Variation in size of
red blood corpuscles Normoblasts were present
Platelet count, 420 000 per c mm Coagulation
time 5 minutes—time is diminished

After June 6th, 1942 several attempts were made
by Dr Chamberlain and myself to obtain speci-
mens of blood for blood urea and other tests, but
the blood clotted immediately in needles and
syringe and in the veins—probably because of liver
changes due to her toxic condition

A sample was obtained on July 20th, 1942, but
even then the veins thrombosed at the pricks and
we believe that there were further thromboses in
the muscles, as there were contractures of both
arms at the elbows and wrists There were also
contractures of the third and fourth digits of the
left hand These were treated by splinting and
later by massage and exercises

Thrombosis of the leg veins caused great diffi-

culty of movement although gradual recovery took place, and the patient was able to get up at the beginning of August

Her blood-urea was 35 mg / 100 c c on July 20th 1942, and 30 mg / 100 c c on August 28th, 1942, and her urea concentration test became normal

She was discharged on August 29th 1942 her condition being very satisfactory, except for some residual contracture of the right elbow

In 1918 Clifford White⁵ described 2 cases of puerperal anuria, in which he incised the renal capsule, and at the operation he removed a small portion of the kidney for section. His patients recovered, and from study of the sections he concluded that "the condition is an acute inflammatory swelling with oedema, which goes on to thrombosis and the necrosis which is

Urine	Blood-urea mg 100 c c blood	Urine S G	Urine urea
May 19th 1942	234	—	—
May 22nd 1942	273	1 006	—
May 25th 1942	356	1 009	0 5 per cent
May 27th 1942	294	1 010	0 5
May 30th, 1942	192	1 010	1 3
June 3rd, 1942	—	—	1 3
June 6th, 1942	86	1 012	—
July 20th 1942	35	—	2 0
July 27th 1942	Urea concentration test (Before taking urea)	—	1 5
		(1 hour later)	2 3
		(2 hours later)	2 8
		(3 hours later)	3 2
Aug 28th 1942	30	—	—

The special interest of these 2 cases lies in the similarity of the sequence of clinical events

Both patients were in the 6th month of pregnancy—after delivery there was a sudden alarming drop in blood-pressure indicating shock. There was haematuria (not confirmed in the first case) but very marked in the second case. This was followed by oliguria and a marked rise in the blood urea. In the fatal case the kidneys showed a complete bilateral cortical necrosis with sub-capsular haemorrhages—microscopically a sub-acute nephritis with no evidence of previous disease

The first description of bilateral cortical necrosis was given by Juhel-Rénoy¹ in 1886, and in 1913 Rolleston² was only able to find 10 authentic cases in the literature. Almost all occurred in pregnancy, and all had a fatal termination

found post-mortem." He considered that the suppression of the urine was due to the marked distension of the tubules and the space round the glomerulus, this causes stasis from which the patient may recover

Crook¹ also incised the capsule in one of his patients with a satisfactory result, and in his sections found a focal necrosis in which the tubules were blocked with secretion and debris, the glomeruli also being necrosed

Gibberd⁵ in 1936 recorded 2 cases of patients recovering from accidental haemorrhage which had in each case been followed by oliguria (or anuria), and raised blood-urea, and described the kidney lesion as being due to engorgement of the blood vessels, followed by thrombosis and necrosis. Kellog⁶ called attention to the frequency with which anuria and oliguria followed premature separation of the placenta and the great danger of this

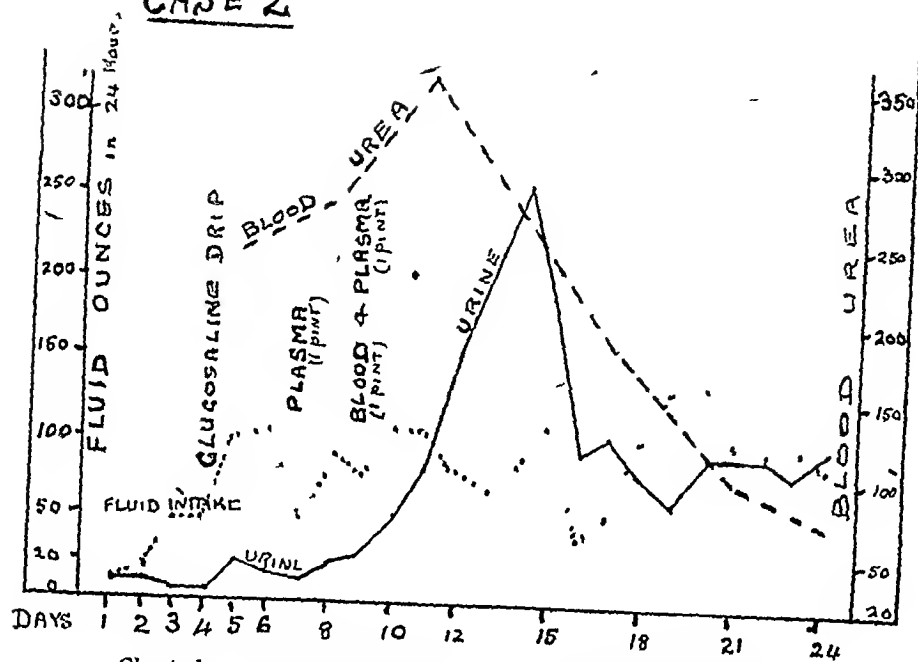
CASE 2

Chart showing intake of fluid, urinary output, and blood-urea

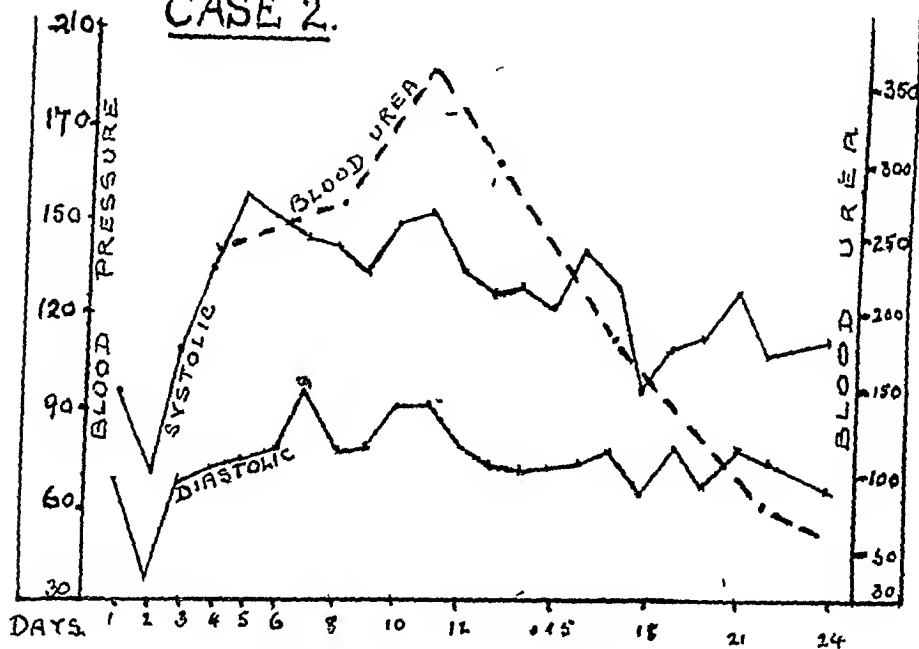
CASE 2.

Chart showing blood-pressure and blood-urea

occurring if the blood-pressure suddenly dropped

In 1941 Lyman Duff and More⁷ collected 71 cases of bilateral cortical necrosis with anuria and azotaemia described in the literature, including 42 surveyed by Ash⁸ in 1933. The cases can be divided into 48 connected with pregnancy, and 23 not associated with pregnancy (including some males)

Of the pregnancy cases, two-thirds were associated with premature delivery, between the 5th and 8th months, or with a stillbirth. Twenty-one of the cases were associated with abruptio placentae and 8 with pre-eclamptic toxæmia.

Of the non-pregnancy cases, the majority were associated with severe infection,^{1 9 10 11 12 13 14 15 16 17 18} or with absorption of toxic substances.^{16 17 18} Duff and More⁷ give a detailed summary of the gross and microscopical descriptions of the affected kidneys.

(a) Areas of necrosis in the cortex, in which, although cortical tissue is clearly recognizable, all components are completely necrotic.

(b) A hyperaemic and haemorrhagic zone on the internal border of the necrotic areas with infiltration of neutrophils and extravasated blood cells.

(c) A thin layer of living tissue separating the area of necrosis from the capsule.

(d) Intra-vascular thrombi and intra-tubular casts.

As early as 1914, Professor James Young¹⁹ put forward the view that a toxæmia of pregnancy evolves during the early stages of placental degeneration, and that the degree of toxæmia is in proportion to the placental lesion, which, in the early stages, is an ischoæmia of the tissue—also that by a consideration of the placenta an approximately correct antenatal history may be described.

In a recent paper²⁰ he suggests that many women, who have toxæmia in the later months, show an "abortion taint" in the early months, and that an increasing damage to placental tissue finally results in a pre-eclamptic toxæmia. A later recrudescence of bleeding (or accidental haemorrhage)—particularly if of the concealed type—by producing an extensive area of damaged tissue, which may involve uterine muscle—may result in anuria and azotaemia.

Delbet²¹ has shown that damage to muscle tissue in severe wounds produces, in the early stages of absorption and disintegration, substances highly toxic to the organism. The concentration of these toxins, in excretion by the kidneys, probably initiates the damage to the renal tubules.

Further light on the aetiology of the kidney damage has been shed by the work of Bywaters and Beall²² and others^{23 24}. They have defined the "crush syndrome," and have described the serious damage inflicted on the kidneys with 48 hours by excretion of bye-products of a severe crush injury of mesodermal tissues, i.e., severe shock frequently out of proportion to the apparent injury, followed by haematuria, oliguria (or anuria) and azotaemia due to damage of the renal tubules and the formation of casts in the lumen.

The pathological changes in the kidneys have been described in detail in a masterly paper by Bywaters and Delory²⁵ who give careful microscopical details of the condition. Professor J. Young²⁰ has pointed out the comparison that may be established between the condition of the kidneys in the "crush syndrome" and in accidental haemorrhage, and suggests that the aetiology is probably the same in each.

A similar picture has been drawn by Leslie Witts²⁶ and others^{27 28} of the

symptoms of the patient and the pathological condition of the kidneys in that outrage of mesodermal tissues—a mismatched blood transfusion

Bratton²⁹ in the *Lancet* describes the microscopical appearance of kidneys of 9 cases of "anuria with casts," i.e. degeneration of tubules with necrosis of individual cells and formation of cellular casts (red blood cells, epithelial cells, leucocytes and blood pigment) with interstitial oedema and foci of sub-acute inflammatory infiltration. Blood vessels were engorged. Seven of these cases were described as "septic abortion" or "abortion with septic spleen," and had a history of anuria (or oliguria) and/or raised blood-urea. The case records given do not show when sepsis began, nor its relation to the anuria, but in the second case described above, the sepsis only appeared on the 7th day, when there was some slight recovery of kidney function. That is, the sepsis here seemed to be merely a complication of the original illness.

A second complication of the illness was a tendency to thrombosis with lowering of the blood coagulation time—a complication noted also by Gibberd⁵. In the account of his treatment of his cases Gibberd used 5 per cent intravenous glucose saline with 50 c.c. of 30 per cent glucose solution every 4 hours, but "due to the injection of the strong glucose solution" it soon became increasingly difficult to find a vein, as there was so much localized thrombosis. Davidson and Turner³⁰ particularly noticed thrombosis of the renal arteries in two of their cases, and suggest that a study of the coagulation time of the blood in these cases might be profitable.

A third interesting case has occurred recently in the wards, in which a damaged placenta was retained *in utero* for some hours with a resulting marked rise in the blood-urea.

The patient, aged 27, was delivered of her first baby in a nursing home. She had had a normal labour and delivery under a short chloroform anaesthesia. Delivery was at 6.15 p.m. At 7.15 p.m. as the placenta had not been delivered, the patient was given 5 units of pitocin and 0.5 mg of ergometrine at 8 p.m. At 10.15 p.m. she was seen by a specialist. He found her in a state of severe collapse and a vaginal examination disclosed that there was a contraction ring below the placenta. He advised immediate admission to hospital.

On admission the patient was found to be in a state of severe shock and collapse. She was cold, restless, with a rapid thready pulse, which at times was almost imperceptible. The blood pressure was 80/60.

On abdominal examination the uterus was felt to be almost stony hard, tightly contracted, tender and lying over to the right. On vaginal examination neither the placenta or cord were felt; the cervix was soft, but the uterine muscle was tightly contracted above.

Shock treatment was given—morphia 1 pint of plasma 1 pint of blood.

Sept 26th, 1942. At 1 a.m. blood pressure 75/56, at 8 a.m. blood-pressure 110/40 at 2 p.m. blood-pressure 110/70, at 8 p.m. blood pressure 130/90.

At 3 p.m. the placenta was removed manually under deep chloroform anaesthesia, was adherent in the right cornu and was very ragged and came out in pieces.

Patient's condition rapidly improved, and a record was kept of intake and output of fluids, but a normal balance was instituted on the first day.

Sept 26th 1942. Blood urea 79 mg/100 c.c. (before delivery of placenta).

Sept 26th, 1942. Plasma potassium 21.8 mg/100 c.c. Blood-pressure 135/85—remained at this level through the week.

Sept 28th 1942. Blood-urea 53 mg/100 c.c. Clotting time 3 minutes 50 seconds.

Oct 1st 1942. Blood urea 42 mg/100 c.c.

Oct 12th, 1942. Patient greatly improved only the pulse rate remained in region of 110-120. Blood-urea 35 mg/100 c.c. Blood pressure 130/80. Urine the deposit contained urates, epithelial cells and some pus cells.

SUMMARY

(1) Two cases are described of oliguria following abortion

Case one Patient with severe pre-eclamptic toxæmia, in whom the added trauma of induced delivery brought about shock and kidney disfunction

Case two A patient who fell, and probably had a traumatic accidental hæmorrhage, which produced hæmaturia, shock and oliguria with azotaemia

(2) A survey of recent literature indicates that possibly a common aetiology of the conditions may lie in a damaged placenta

(3) Two noteworthy complications have been described

(4) A third case is described, in which injudicious use of oxytocic substances caused the uterine muscle to contract tightly on a partly-adherent placenta, causing severe shock with marked rise in blood-urea

I am indebted to Mr Norman Pitt for permission to publish these cases, and to Professor Young for his valuable advice

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Reactions to Pressor Substances in Normal and Toxaemic Women

BY

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In 1937 Shockaert and Lambillon¹ published the results obtained by intravenous injection of a pressor substance, tonephin (an extract of the posterior pituitary lobe) in normal women not pregnant, and normal pregnant and puerperal women, and in women who had pre-eclamptic toxæmia. In normal women who are not pregnant an average rise of 45 mm Hg occurred in the systolic arterial blood-pressure. In normal pregnant women in the last 3 months the corresponding rise was 13 mm Hg, while in patients who had pre-eclamptic toxæmia it was 55 mm Hg. At the same time there were general reactions on the part of the patients to the injections which differed considerably in the 3 groups. In the women not pregnant the phenomena were very severe. Some seconds after the injection extreme pallor was noted and the lips were cyanosed, respiration was accelerated, there was dyspnoea and at the same time the patient had an indefinable sense of malaise, followed by nausea and even vomiting, and abdominal pains, with desire to empty the bowels or to pass urine. There were often cold sweats with small feeble pulse. These phenomena lasted for 7 or 8 minutes and then gradually passed away. In the normal pregnant women they were much less severe and might be almost entirely absent, and those that were present disappeared quickly—usually in 2 or 3 minutes.

From these observations Shockaert and Lambillon argued that there must be

present in the serum of the normal pregnant woman, especially in the later weeks of pregnancy, some substance antagonistic to tonephin. In pre-eclamptic toxæmia, though such a marked rise occurred in the systolic blood-pressure the general reaction was less severe than in the women not pregnant but more severe than in the normal pregnant woman. In the puerperium they found that the refractoriness to tonephin, that had characterized the normal pregnant woman, disappeared rapidly so that by the 9th day of the puerperium the rise of blood-pressure and the general reactions were similar to those obtained in the normal woman not pregnant. The mean rise of systolic blood-pressure in normal puerperal women was 44 mm Hg, i.e. practically the same as that in the normal woman not pregnant.

In the same year Dieckmann and Michel published the results obtained by subcutaneous injection of pituitrin in 16 normal and 19 toxæmic women. In the former an average rise in the systolic pressure of 11 mm Hg was obtained, while in pre-eclamptic toxæmia the average rise was 51 mm Hg. From this high rise in pre-eclamptic toxæmia and also from the fact that the injection caused a marked decrease in the volume of urine they argued that the posterior lobe of the pituitary had something to do with the causation of the disease. Too much secretion may be produced or there may be some defect in its neutralization, or the woman might be

unduly susceptible to its action In "vascular renal disease" in pregnancy the reaction obtained was similar to that in the normal pregnant woman, viz, 7 mm Hg, and they therefore suggested the test as a means of differentiating this condition from pre-eclamptic toxæmia

In 1938 de Valera and Kellar³ published the results of tonephin injections in a similar variety of cases to those studied by Shockaert and Lambillon Their results were on the whole very similar For purposes of comparison the three sets of results are shown in Table I

The comparable figures obtained by the author are given in column 4

more or less frequent intervals until the base level was reached This took from 30 to 45 minutes The pulse-rate at this time was also recorded Tonephin (Bayer) 0.66 c.c. was then injected slowly into an arm vein Systolic and diastolic blood-pressure were then recorded at first at intervals of 30 seconds or thereabouts, and later less frequently until the base level was again reached The time taken to reach the base level was noted Throughout the experiment the objective reactions were noted, including the pulse-rate and after it the patient was questioned regarding her sensations In addition, therefore, to notes of the general reaction records were

TABLE I
*Reactions to Pressor Substances (Rise of Systolic Arterial Pressure in mm Hg)
in Normal and Toxaemic Women
(Comparative Results of Various Workers)*

	Shockaert and Lambillon (Tonephin)	Dieckmann and Michel (Pituitrin)	de Valera and Kellar (Tonephin)	Browne (Tonephin)
Normal women not pregnant	45	—	35	21.3
Normal pregnant women	13	11	23	33.2
Pre-eclamptic toxæmia	55	51	43	54
Pregnancy with chronic hypertension	16*	7.7	—	53
Normal puerperal	44	—	44	48.2

* It is doubtful whether these are the same kind of case that I classify as "hypertensive" Shockaert calls them *femme brightique* Possibly they are examples of chronic glomerular nephritis

It will be seen that while the figures are in most respects similar there are certain important differences In view of these it was decided to repeat the experiments and that to eliminate so far as possible the personal factor they should all be done by one worker (myself) The method used was as follows The subject, at a time as far distant from her last meal as possible, was placed recumbent on a couch or bed After a short period of rest her blood-pressure was taken and the estimation repeated at

obtained of the rise of systolic and diastolic blood-pressure and of the time taken for their return to normal In a certain proportion of all except the puerperal patients cold pressor tests (by putting the hand and forearm in an ice bath) were also carried out for purposes of comparison Finally in many of the patients tonephin tests were repeated in the puerperium—in some two or three times As the experiments have occupied the last 2½ years they extended over the worst periods of the air attacks

on London, and as many of the women were evacuated to distant places in the country prolonged follow-up in the puerperium was often impossible. As will be seen later the reactions of these patients in the puerperium offer an interesting and possibly a fruitful field for investigation.

The results of the tests including the mean rises of systolic and diastolic blood-pressure, standard deviations (S D), range, and time taken to return to normal levels are shown in Tables II to VI.

obtained. The mean systolic rise was 21.3 mm Hg (Table II).

Normal pregnant women (20 cases). Most were at term or near it and none was under 35 weeks. All were healthy before pregnancy, none had albuminuria or oedema at any time and the highest blood-pressure reached during pregnancy had not exceeded 130/70. The mean systolic rise was 33.2 mm Hg (Table III).

Preeclamptic toxæmia (20 cases). Full details of these, including the signs of

TABLE II
Summary of Reactions to Tonephun and Cold Pressor Tests in Normal Pregnant Women
(24 cases)
(Reactions are in mm Hg and the time in minutes)

	Mean rise in systolic blood pressure	S D	Mean range	Mean rise in diastolic blood-pressure	S D	Mean range	Mean time till normal
Tonephun tests (24 cases)	21.3	9	3-37	24.3	9	10-45	5.6
Cold tests (8 cases)	21	7.4	10-32	21.7	6.2	10-30	7.5

TABLE III
*Summary of Reactions to Tonephun and Cold Pressor Tests in Normal Pregnant Women
and in their Puerperium* (20 cases)
(Reactions are in mm Hg and the time in minutes)

	Mean rise in systolic blood pressure	S D	Mean range	Mean rise in diastolic blood-pressure	S D	Mean range	Mean time till normal
Tonephun tests (20 cases) (Pregnancy)	33.2	13.3	7-60	20	7.9	0-30	8
Cold tests (10 cases) (Pregnancy)	23.1	8.6	9-44	20.5	7.3	7-30	5.5
Tonephun tests (3 cases) (Puerperium)	49	10.8	32-58	39	5.5	34-45	6.5

The most important results may be summarized as follows.

Normal women not pregnant (24 cases). All these were healthy young women in their early twenties who had never been pregnant. In each case the day of the menstrual cycle on which the test was made was noted but this did not seem to have any constant or striking effect on the result

toxæmia present, are shown in Table VII, which also shows the reactions obtained by the cold pressor tests in a number of cases and the results of further tonephun tests in the puerperium. The mean systolic rise during pregnancy was 54 mm Hg (Table IV). In many cases the rise is maintained in the puerperium.

Pregnancy with chronic hypertension

TABLE IV

Summary of Reactions to Tonephm and Cold Pressor Tests in Pre-eclamptic Toxaemia and in their Puerperium (20 cases)

(Reactions are in mm Hg and the time in minutes)

	Mean rise in systolic blood pressure	S D	Mean range	Mean rise in diastolic blood pressure	S D	Mean range	Mean time till normal
Tonephm tests (20 cases) (Pregnancy)	54	19.1	12-79	38.1	18.3	12-79	11.5+
Cold tests (9 cases) (Pregnancy)	19.2	10.4	4-40	19.7	13.2	0-48	8
Tonephm tests (14 tests on 10 patients) (Puerperium)	52.8	15.3	30-86	36.7	12.4	10-60	12

TABLE V

Summary of Reactions to Tonephm Tests in Normal Puerperal Women (20 cases)

(Reactions are in mm Hg and the time in minutes)

Mean day of puerperium	Mean range	Mean rise in systolic blood-pressure	S D	Mean range	Mean rise in diastolic blood-pressure	S D	Mean range	Mean time till normal
10	5-20	48.2	10.75	32-68	42.4	10.2	20-60	10+

TABLE VI

Summary of Reactions to Tonephm and Cold Pressor Tests in Pregnant Women with Chronic Hypertension and in their Puerperium (8 tests on 7 patients)

(Reactions are in mm Hg and the time in minutes)

	Mean rise in systolic blood-pressure	S D	Mean range	Mean rise in diastolic blood-pressure	S D	Mean range	Mean time till normal
Tonephm tests (8 cases) (Pregnancy)	53	11.4	30-62	25	9.9	14-40	11
Cold tests (6 cases) Pregnancy	46.1	9.9	27-55	21.7	10	12-42	8
Tonephm tests (3 cases) (Puerperium)	60	10	48-75	36	12.4	20-60	6.5

(8 tests on 7 patients) In these patients chronic hypertension had existed before pregnancy. There are few patients in this series partly because they are somewhat scarce, but partly also because it was not considered fair to carry out the test on some of the worst cases lest the life of the foetus might be endangered. The mean systolic rise was 53 mm Hg (Table VI).

Normal puerperal women (20 cases)

c

None of these had suffered from pre-eclamptic or any other form of toxaemia during pregnancy and the blood-pressure had not, at any antenatal examination, exceeded 130/70. The day of the puerperium on which the test was done varied from the 5th to the 17th and the average was 10. The mean systolic rise was 48.2 mm Hg (Table V).

DISCUSSION

It will be seen that the results differ materially from those obtained by Shockaert and Lambillon. One of the most striking differences is in the increases of systolic pressure in normal women not pregnant, and normal pregnant women. Evidence was not found of the presence of any inhibitory substance such as was predicated by these authors, and by de Valera and Kellar. Indeed the systolic rise in the normal pregnant woman is significantly greater than in the normal woman not pregnant. Does this mean that some sensitizing substance is present in normal pregnancy that is absent in the nullipara? If this is so one naturally thinks of the experiments of Byrom¹ who produced lesions in albino rats closely resembling those of eclampsia, by injecting vaso-pressin. He also found that the sensitivity of the rat to vaso-pressin could be increased tenfold by preliminary treatment with oestrogenic hormone, and that in unspayed rats the sensitization could equally well be brought about by gonadotropic hormone.

All the workers including the author are agreed as to the great and significant increase in systolic pressure obtained in pre-eclamptic toxæmia. A reference to Table VII will show that it occurred in almost every case. Regarding the cause of it one can again only speculate and again Byrom's experiments are suggestive. Smith and Smith claim to have found an increase of prolactin in pre-eclamptic toxæmia but their results have been severely criticized by Taylor and Scadron² who did not find any constant increase. Taylor and Scadron however agree that oestrin is diminished in toxæmias. It might also be suggested that in women who suffer from pre-eclamptic toxæmia there is a personal or familial predisposition to hypertension and hence to hypersensitiveness to pressor

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substances. This was strongly suggested by the results of cold pressor tests carried out by the author and published in 1940.³ If it is so it is remarkable that no such high reaction occurred in any of the 24 normal young nulliparae on whom tests were done.

It is of great interest to note that the high reactions to tonephin in patients with pre-eclamptic toxæmia are maintained in the puerperium. Whether this is a permanent change is not yet known. In one of the patients (see Table VII) it had diminished considerably by the 52nd day of the puerperium but in another it was still present on the 235th day—the longest time that any one of these patients has so far been followed up. It may be that it is a hypersensitivity characteristic of patients who will later in life develop hypertension. The latter explanation seems to be untenable in view of the fact already mentioned that none of the 24 normal young nulliparae gave a very high reaction. According to Robinson and Brucer⁴ 40 per cent of the population are actual or potential hypertensives, i.e. will, if they survive, and apart altogether from pregnancy, develop hypertension. It is somewhat unlikely, therefore, that not one of these women is a potential hypersensitive.

The high reactions obtained in the puerperia of women who had had normal pregnancies are also very striking. The mean systolic rise of 48.2 is significantly greater than those found in normal pregnancy and much greater still than those in the normal nulliparae not pregnant. It will be noted however (Table I) that only slightly lower values for the normal puerperium were obtained by Shockaert and Lambillon and by de Valera and Kellar. The cause of this increased sensitivity after delivery is not known, nor how long it lasts. In one case it was still present on the 20th day of the puerperium and in two others

on the 17th day. Withdrawal of progestin after delivery might be suggested but work has not yet been done to prove or disprove this view and Byrom found that the sensitization in rats caused by oestrogenic substances could not be prevented by progesterone.

It will be noted (Tables IV and VI) that the mean systolic rise with Tonephin was similar in pre-eclamptic patients and in those with chronic hypertension in pregnancy, and that both were very high, but that the reactions to the cold test were different. In pre-eclamptic toxæmia the reaction to the cold test was low (mean systolic rise 19.2 mm Hg) while in the chronic hypertensives it was high (46.1 mm Hg). It is possible, therefore, that the cold test might be of value in differentiating these two conditions.

Shockaert and Lambillon laid great emphasis on the differences in the general reactions obtained in the various groups, especially in supporting their view that an inhibitory substance was present in normal pregnancy which was absent in the non-pregnant. In the present series the reactions were very variable and unpredictable, and as the changes caused were mostly subjective (pallor, faintness, cold sweats, pulse slowed or rapid and weak, numbness, abdominal pains, headaches, etc.) they could rarely be accurately measured. The general reaction often seemed to bear little or no relation to the amount of elevation of the blood-pressure.

SUMMARY AND CONCLUSIONS

1 This paper deals with the results of tonephin injections and cold pressor tests in a series of healthy nulliparae not pregnant, normal pregnant women, normal puerperal and toxæmic women.

2 Evidence has not been found of the presence of an inhibitory (antipressor) sub-

stance in normal pregnant women. Rather does it appear that a sensitizing substance may be present in normal pregnancy that makes the patient more sensitive to pressor substances than the non-pregnant woman.

3 The pre-eclamptic patient is much more sensitive to the action of pressor substances than either the normal non-pregnant or the normal pregnant woman. Some of the possible reasons for this are discussed.

4 A similar hypersensitivity is present in the patients with chronic hypertension in pregnancy, i.e. patients in whom chronic hypertension existed before pregnancy.

5 The hypersensitivity characteristic of the patients with pre-eclamptic toxæmia continues in the puerperium and has been found as late as its 235th day. Whether it is permanent or not is not known, neither is it known if it is universal.

6 The same hypersensitivity is present in the normal puerperal woman who has had a normal (non-toxæmic) pregnancy. This has been found as late as the 20th day of the puerperium.

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Delivery of the Foetal Head in Occipito-Anterior Positions of the Vertex

BY

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SPEAKING in Manchester some 10 years ago, the late Professor Blair Bell, after referring regretfully to the fact that so many women died as a result of childbearing, declared "Since these deaths are tragedies where there should be rejoicing in the consummation of a natural event, it comes about that even though the mother escape with her life this happy issue is liable to obscure subsequent disabilities which persist, sometimes to "dog her footsteps" for life. It is the urgent, the dramatic, that affects the long-drawn-out is too often regarded as inevitable—a pleasing alternative to "something worse." "The woman damaged by childbirth" (to quote Professor James Young) is a constant reminder of our shortcomings in maternity practice, and of the urgent need for redoubled efforts to reduce the incidence of maternal disablement, and my study has been undertaken with this object in view. Again in the words of Blair Bell "There is ample room for improvement among the most proficient, and this is related chiefly to perfection of technique and the application of correct procedure, all of which require thought, and then further thinking."

THE MECHANISM OF LABOUR

Owing to the comparatively small size of the birth canal in relation to that of the mature foetal head, it is apparent that all

sectional planes of the head will not readily pass through the canal, and that some process of adaptation or accommodation will be necessary before the birth of the child can take place. The series of movements which facilitate the passage of the foetus through the maternal canal and the mechanical factors responsible for their occurrence are referred to as the mechanism of labour. A knowledge of certain anatomical facts about the parturient canal and the foetal head is essential to a full understanding of this mechanism and its practical application to the management of labour.

The genital tract in the non-pregnant state may be looked upon as a potential elastic channel which will not be completely opened until the largest disengaging plane of the foetal presenting part is lying in the vaginal orifice. During pregnancy the uterus enlarges progressively and, in the course of labour, the lower uterine segment is expanded and the cervix, vagina and vaginal orifice are dilated as the foetus is advanced. When the vagina is distended, the perineum is depressed, elongated and broadened, the anus is dilated and the anterior segment of the obstetrical perineum, between the posterior labial commissure and the anterior anal margin, is greatly thinned and stretched, its muscles being displaced posteriorly and laterally. The posterior ano-coccygeal segment of the perineum is also under tension and the

coccyx is extended. The expanded parturient canal, the passage through which the foetus must be driven during birth, may therefore be described as a cylindrical canal, circular in cross-section and curved on the antero-posterior plane. Only its upper half lies within the bony pelvic cavity. Its anterior internal surface is short and convex, its posterior internal surface is long and concave, and its axis is a curved central line corresponding with the axis of the pelvis in its upper and a continuation of this curved line in its lower segment.

The cavity of the true pelvis in the living subject is upholstered with muscles which also assist the aponeurotic, fascial and neuro-vascular structures to close the inter-osseous spaces. This muscular layer reduces the available diameters of the basin and helps to convert it into the rigid cylindrical channel through which the upper part of the parturient canal passes. The suspensory and supporting structures of the pelvic diaphragm, of which the most important in relation to our study are the superficial fibro-muscular and cutaneous tissues of the anatomical perineum, the musculature of the pelvic floor, and the pelvic fasciae, bridge and almost close the pelvic outlet.

The anatomical perineum, which includes all those structures covering the pelvic outlet, may be divided into the urogenital and anal triangles. These have a common base on the bis-ischial diameter, which crosses the perineum immediately in front of the anus. The obstetrical perineum lies between the posterior labial commissure and the coccyx. Beneath the cutaneous tissues of the urogenital triangle are the superficial perineal muscles, the rigid uro-genital diaphragm and its contents which are pierced by the urethra and vagina, the former, thickened by the presence of its intrinsic sphincter in its upper third, lying in close relation to the anterior vaginal wall. The

bulbo-cavernosus acts as a sphincter for the vaginal orifice, the sphincter urethrae membranaceae compresses the urethra, and the transverse perineal muscles fix the central tendinous point of the perineum. In the anal triangle lie the anal canal with its sphincters and the fibro-fatty supporting tissues of the ischio-rectal space.

The muscular layer of the pelvic floor consists of the levator ani, the coccygeus (ischio-coccygeus) and the pyriformis on either side and, apart from the urogenital aperture between the levatores ani in front, closes the pelvic outlet. Each levator ani consists of two parts, the ilio-coccygeus, which arises chiefly from the lateral pelvic wall at or near the white line to be inserted into the lower sacrum and coccyx and supports the pelvic and abdominal viscera, and the pubo-coccygeus, which arises from the back of the pubis and anterior part of the white line, forms the lateral margin of the uro-genital aperture, and is inserted into the perineal body, the ano-coccygeal raphe, and the coccyx. Its anterior fibres, of which only a small number pass in front of the anal canal to the central point of the perineum, form the pubo-rectalis muscle which acts as a powerful sphincter for the urogenital aperture. During the 2nd stage of labour the pubo-rectalis encircles the lower part of the parturient canal in the pubo-anal plane, its anterior fibres having maintained their normal relation to the bis-ischial diameter.

The deep intra-abdominal fascia, which lines the muscular and bony walls of the abdomen and pelvis, splits into three layers at the origin of the levator ani on either side. One descends caudally to line the lateral wall of the ischio-rectal space, the second covers the inferior surface and the third the superior surface of the levatores ani and coccygei muscles. The endo-pelvic fascia is in continuation with the sub-peritoneal tissue and overlies the deep fascia

above the levatores ani. It is a loosely woven connective tissue which covers the upper aspect of the pelvic floor and invests the pelvic viscera not covered by peritoneum above this level. Condensations of this fascia develop in lines of stress, usually in relation to blood vessels, to give additional support to the viscera. The most important of these are the anterior and lateral true ligaments of the bladder, the post-vesical fascia, the transverse cervical ligaments, the utero-sacral ligaments and the rectal fascia. The anterior true ligaments of the bladder constitute, with the post-vesical fascia, the pubo-cervical fascia. These condensations have a considerable admixture of elastic and muscular tissue, giving them a resilience and contractility which aids their supporting function.

The foetal head may be looked upon as a solid semi-paraboloid body with a plastic vault and rigid base, the latter being joined by the flexible neck to the trunk. Its size is variable, but the following table will give the average dimensions in inches of the more important planes of the un-moulded skull of a 7-pound foetus together with a concept of their relative sizes.

hinge-like movement and overriding of the bones at the sutures, and possibly by a minor reduction in size of the skull by expression of small quantities of cerebro-spinal fluid and of venous blood from the cranial cavity. The brain itself is incompressible but the medulla may sometimes be depressed into the foramen magnum. The degree of moulding is proportional to the constraining force to which the head is subjected and its resistance to compression primarily depending upon the degree of ossification of the cranial bones and the strength of the dural septa. When the tenacity of the dural septa is exceeded, rupture occurs and there is a considerable risk of intra-cranial haemorrhage. As the diameters of the engaging plane of the foetal head are shortened there is a compensatory lengthening of the diameter corresponding with the axis of that plane and which lies in the axis of the birth canal. Thus the vertico-mental diameter is elongated when the sub-occipito-bregmatic plane is engaging, the sub-mento-vertical diameter when the occipito-frontal plane is engaging, and the sub-occipito-bregmatic diameter when the

PLANES OF FOETAL SKULL

Name	Diameters	Circumference	Area
Sub occipito-bregmatic	$3\frac{3}{4} \times 3\frac{3}{4}$	$12\frac{1}{4}$	9
Sub-occipito frontal	$4 \times 3\frac{3}{4}$	13	$11\frac{1}{4}$
Occipito frontal	$4\frac{1}{2} \times 3\frac{3}{4}$	$13\frac{1}{2}$	$13\frac{1}{4}$
Occipito mental	$4\frac{1}{2} \times 3\frac{3}{4}$	$13\frac{1}{2}$	$13\frac{1}{4}$
Vertico-mental	$5\frac{1}{2} \times 3\frac{3}{4}$	$14\frac{1}{2}$	$16\frac{1}{4}$
Sub mento-vertical	$4 \times 3\frac{3}{4}$	13	$11\frac{1}{4}$
Sub occipito mental	$3\frac{3}{4} \times 3\frac{3}{4}$	$12\frac{1}{4}$	9

During its propulsion through the maternal passages in the course of labour, the foetal head is subjected to compression by the resistant and resilient walls of the parturient canal and this effects a certain alteration in the shape of the vault of the foetal skull which is brought about by a

vertico-mental plane is engaging.

A secondary modification in shape of the foetal head is caused by the development of the caput succedaneum on the leading unsupported part of the scalp due to pressure during uterine contractions against a relatively indistensible ring, the dilating

cervix in the case of the primary caput and the vaginal canal or ostium for the secondary caput. Either or both may be enlarged in cases of prolonged or obstructed labour, according to the level of the arrest of the head in the birth canal.

In occipito-anterior positions of the vertex the flexed foetal head is driven into the birth canal during labour as the lower uterine segment is expanded and the cervix is withdrawn. The longitudinal diameter of engagement, with the occiput to the front usually occupies one or other of the oblique diameters of the pelvic brim but may sometimes enter its transverse diameter. Flexion normally increases during early descent of the head and the sub-occipito-bregmatic sectional plane is brought into the normal sectional planes of the birth canal at the various levels of the girdle of contact. Deflexion results in the engagement of larger planes, thus the occipito-frontal is 47 per cent and the verticomenal 80 per cent greater in area than the sub-occipito-bregmatic plane. The bladder is usually elevated with the lower uterine segment into the abdomen. During the second stage the foetal head advances within the vagina with each contraction and recedes during relaxation, and in addition the vaginal wall at the girdle of contact and in advance of the foetal head is driven down during the contraction and returns to its original position in the interval of rest. The major axis of the foetal head, at right angles to the plane of engagement, tends to pass into the axis of the parturient canal. When these axes correspond, resistance to further progress is minimal. This movement, considered in relation to the antero-posterior diameters of the canal, constitutes internal rotation, and, in relation to the transverse diameters, extension of the foetal head. Internal rotation and primary (pre-crowning) extension of the foetal head may therefore be

looked upon as different aspects of a single movement designed to bring the major axis of the foetal head into that of the birth canal.

Internal rotation of the foetal head through one-eighth or one-quarter of a circle brings the occiput beneath the subpubic arch, and results from the operation of a number of interrelated factors. It is most likely to take place when the uterine propulsive force is adequate, the birth canal will dilate to form an intact curved cylindrical channel, the foetal passenger is proportionate to the maternal passage, which will offer adequate elastic resistance to its descent, the foetal head is well flexed at an early stage of labour, moulded in this attitude of flexion and capped by a caput succedaneum to convert it into a semi-paraboloid form with a flexible attachment at the neck to the cylindrical trunk, lateral inclination is easier than further flexion of the already fully flexed head, which tends to extend and reoccupy a position of rest in relation to the trunk. Deflexion of the head results in angulation between the head and trunk which converts the forepart of the foetus into an asymmetrical body convex anteriorly and concave posteriorly, a shape which facilitates the completion of its internal rotation and progress through the lower curve of the birth canal. Conversely rotation is likely to be delayed and incomplete in the presence of uterine inertia, perineal deficiency, a small foetus and a spacious, atonic birth canal, incomplete flexion, premature extension, non-moulding or abnormal moulding of the foetal head, and foetal atony or rigor mortis due to intra-uterine death. Under favourable conditions, primary extension of the head commences in cases of occipito-posterior position as soon as the occiput rotates in front of the transverse diameter of the pelvis, and therefore as soon as internal rotation commences in

cases of occipito-anterior position. At first the amount of extension is slight, but as internal rotation is nearing completion the movement is greater, and it ceases when the mento-vertical axis of the head corresponds with the axis of the birth canal. This primary extension of the head is brought about by extension of the cervical spine as a whole and, unlike secondary extension, is not a simple hinge-like movement at the atlanto-occipital joint. The head is deflexed, the vertex is thrust forwards towards the vaginal outlet, the cervical spine is opposed to the posterior surface of the pubes and the occiput is freed beneath the pubic arch. If primary extension did not take place and complete flexion was maintained, delivery could be effected only by direct advance of the foetal head through the centre of the pelvic floor, the head being unable to negotiate the curve of the birth canal.

As the presenting-part advances the obstetrical perineum is expanded, the anus becomes turgid and dilates to expose a D-shaped area of the anterior wall of the anal canal, and the vaginal orifice, the least distensible part of the vaginal canal, is gradually stretched. The scalp overlying the postero-medial angles of the parietal bones first appears at the vaginal orifice and, as the head is crowned, the occiput is freed beneath the pubic arch and the anterior part of the vertex distends the anterior margin of the perineum, which is markedly thinned. A small posterior laceration of the fourchette which usually bleeds freely may be considered inevitable in primiparae at this stage. The sub-occipital region, between the superior nuchal lines and the posterior margin of the foramen magnum becomes fixed below the pubic rami as the distended perineum resists further caudal descent of the vertex, and the head begins to pivot around the sub-occipital point. This is the mid-point

of the sub-occipital region which lies in contact with the anterior margin of the vaginal orifice and below the symphysis pubis and represents the nearest accessible point to the atlanto-occipital joint. The urethra lies in the triangular recess bounded by the medial borders of the pubes and the sub-occipital region of the foetal skull and therefore escapes damage. The frontal and facial regions pass over the perineum in turn to complete the birth of the head, the disengaging planes being the sub-occipito-bregmatic, sub-occipito-frontal and sub-occipito-mental. Secondary extension is brought about by the removal of the resistance to ascent of the free occiput after crowning, when caudal pressure causes the frontal end of the head lever to descend, and by the resultant force of the *vis a tergo* of the uterus and the reactionary force of the perineum driving the head forwards and upwards. If the vaginal outlet is inadequate in size to permit the passage of the disengaging head or secondary extension commences before the occiput is born, laceration of the perineum and posterior vaginal wall may result, these parts being more vulnerable than the anterior vaginal wall as the long posterior concave wall of the birth canal lies in the direct line of force through the advancing foetus. The risk of laceration is increased when the sub-pubic angle is acute and the head is necessarily displaced backwards towards the coccyx, and of damage to the attached muscles and ligaments when the coccyx is over-extended. Premature extension of the head would increase the area of the largest disengaging plane by 13 per cent, the occipito-frontal replacing the sub-occipito-frontal plane.

THE MANAGEMENT OF LABOUR

The purpose of assistance at delivery of the foetal head is to aid the series of move-



FIG 1

Diagrammatic representation of the progress of the foetal head through the birth canal (Adapted from Ten Teachers Midwifery)



FIG 2

Birth of the foetal head showing the disengaging diameter before the occiput has been freed from the vestibule (Adapted from Stander and Williams)

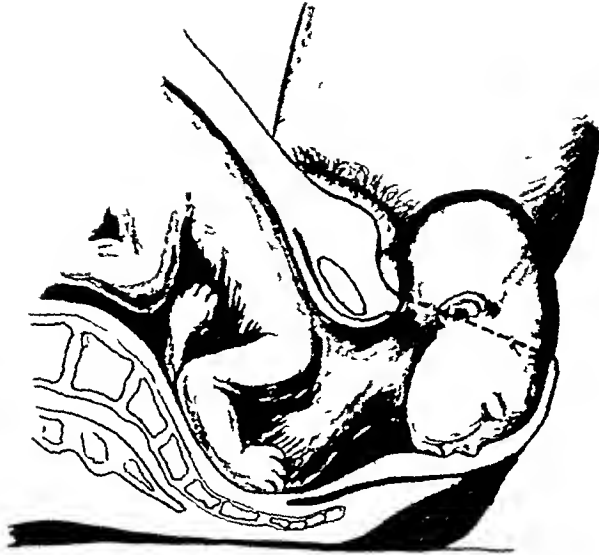


FIG 3

Birth of the foetal head showing the disengaging diameter after the occiput has been freed from the vestibule
(Adapted from Stander and Williams)

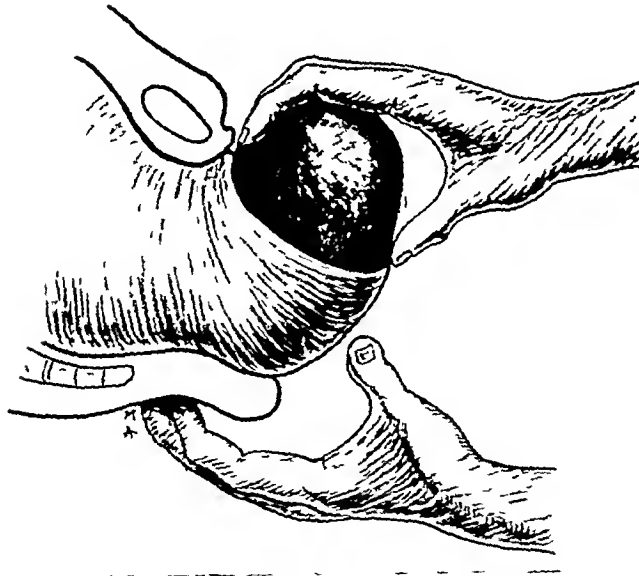


FIG 4

Completion of the forward thrust of the foetal head in primary extension aided by ano coccygeal pressure (Adapted from Bumm)



FIG 5

A case of stress incontinence of urine showing a healed anterior vaginal laceration and an intact perineum

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ments which constitute the mechanism most favourable to the successful termination of labour with minimal damage to the mother and child

The choice of position for the patient during the second stage of labour is of some importance. Probably the most satisfactory attitude to adopt before the presenting part appears at the vulva is the exaggerated lithotomy position, the patient grasping the knees of her flexed and widely separated legs and straining as at stool during pains. This is inferior only to the squatting position as a means of using the accessory powers to best advantage and has the additional merits that it is less trying to both patient and attendant than the majority of the alternative attitudes. She should not tense her adductor or pelvic floor muscles, as this may delay the advance of the foetal head and increase the risk of damage both to the pelvic floor and to the intra-cranial structures, and she should rest with her feet on the bed between contractions. In occasional cases, if the patient is nervous and rigid, local perineal anaesthesia may assist relaxation and co-operation may be rendered more satisfactory. As soon as the presenting part appears at the vaginal orifice the patient is put into the position chosen for delivery, the bladder having previously been emptied.

The chief considerations in the choice of suitable delivery position are practicability, accessibility, relief of perineal tension and non-interference with the normal course of labour. Thus Sims' position is unsuitable owing to the difficulty in maintaining asepsis and control of the patient, the squatting position is impracticable owing to the inaccessibility of the parts, to increased perineal tension, and to anaesthetic difficulties, and the exaggerated lithotomy position owing to increase of perineal tension due to leg flexion. The

two most satisfactory and convenient positions for delivery are the dorsal position with the legs semi-flexed and the knees apart, and the left lateral position with the right leg raised and semi-flexed and the left leg straight or nearly so. In the former the work of the assistant is less arduous and the patient need not be moved immediately after delivery, but the perineum is less accessible, the hand extending the head through the perineum is more liable to be contaminated from a soiled bed and, at a later stage, there is less freedom of movement for delivery of the anterior shoulder. In the latter, an assistant is fully occupied in supporting the left leg and, in domiciliary practice, the only assistant is usually required to devote all her full attention to the administration of the anaesthetic at this stage. The choice between these two positions usually depends upon the circumstances of the specific case under consideration.

The attendant should now stand at the right side of the bed facing the vulva. Both hands should be free, and the practice of passing the left arm around the right thigh of a patient lying in the left lateral position is to be condemned as the observance of strict asepsis is embarrassed, the control of the head before and during delivery is unsatisfactory, and withdrawal of the hand is necessary as soon as the head is born for the toilet of the eyes and upper respiratory passages, and for delivery of the shoulders and trunk. The patient takes a deep breath and, fixing the diaphragm and grasping the bed, a sling attached to the foot of the bed, or the hands of an assistant, bears down strongly and repeatedly so long as the pain lasts. Three or four sustained "bearing-down efforts" will effect a much more satisfactory advance of the head than multiple, brief, spasmodic attempts to strain. Co-operation is usually assisted by the judicious use of light, inter-

mittent anaesthesia, and the patient should rest between contractions

The use of vaginal lubricants is not recommended when the foetal head has reached the pelvic floor, but a small quantity of undiluted Dettol or Dettol cream is usually put on the fingers before necessary vaginal examinations during the course of labour and this may help to reduce the delaying effects of friction upon the advancing head. Lubricants applied in advanced labour render the grasp by the hands of the attendant on the foetal head less secure and its control more difficult. As the perineum is expanded and the head is crowning the fingers of the right hand should be placed behind the occiput and the thumb near to the anterior fontanelle in order that the risk of a rapid, uncontrolled, surprise advance of the head, with its attendant risk of laceration of the perineum, may be obviated. A sufficient degree of flexion should be maintained to keep the axis of the foetal head in that of the lower strait of the vagina. When in doubt about the degree of flexion which should be effected, it may be useful to remember that premature extension is usually more harmful at this stage than delayed extension, and therefore it is wise to err on the side of over- rather than under-flexion. When necessary, completion of internal rotation may be assisted by gentle manual rotation of the flexed head between contractions to carry the anterior fontanelle towards the posterior vaginal wall and holding it in that position until the next contraction fixes it. This manoeuvre is usually unnecessary when adequate time is allowed for perineal distension, but in certain cases may materially assist the progress of labour.

As the occiput is disengaged from the pubic ramus it should be freed from the anterior margin of the vaginal orifice by displacing the vestibule and labia minora to the nape of the neck. In a well moulded

or dolicocephalic head, and, to a lesser degree, in a normal unmoulded head, this will expose a considerably greater area of scalp in the occipital region, will bring disengaging planes of smaller area through the vaginal orifice, will reduce the risk of damage to the anterior vaginal wall, the uro-genital diaphragm, and its contents, including those responsible for urinary control, and will relieve perineal tension. Manual "ironing" of the perineum is more liable to cause trauma than natural distension by the foetal head and increases the risk of concealed laceration of the perineal body. When necessary, if the uterus is contracting powerfully, the advance of the head may be retarded to allow gradual stretching of the perineum to occur by inducing the patient to refrain from violent bearing down efforts, the careful use of general anaesthesia and support of the exposed vertex by the right hand. Pressure on the head through the perineum greater than is necessary to maintain adequate flexion may increase the risk of damage to the pelvic floor and is therefore unsuitable for restraining the head. No true "support" is afforded to the perineum by direct pressure, except by retarding the advance of the head, therefore it is more reasonable to support the head by pressure on the scalp itself rather than on a vulnerable medium already under tension. In no case should labour be obstructed by preventing advance of the foetal head without lessening the *vis a tergo* from a powerfully contracting uterus by general anaesthesia. If a uterus is contracting strongly the force directed against the perineum is less when the patient is in the left lateral than in the supine position so the former is more suitable when contractions are too powerful, and vice versa. Howat states that the head should advance about half an inch with each pain as the perineum begins to stretch and about one quarter of an inch

when the head is crowned. This may be taken as a guide to the progress which may be considered satisfactory. If the second stage of labour is unduly prolonged the cumulative effect of repeated advance and retreat of the foetal head may result in permanent overstretching of the vaginal wall and its subjacent structures, especially the urethra and its sphincters. Further, the lower vagina is normally softened by venous congestion and may become oedematous and more susceptible to trauma in prolonged labour. As the head advances the occiput is again freed from the vestibule and the bi-parietal, the longest disengaging transverse diameter, escapes from the vaginal orifice as secondary extension commences. At this stage the foetal brow may usually be palpated through the ano-coccygeal segment of the perineum, and the head may be fixed in its position of maximal descent by pressure of the fingers of the left hand, palmar surface forwards, in this region during a contraction and held in that position until the uterus relaxes. This pressure will also complete the forward thrust of the foetal head which accompanies primary extension. As soon as this fixation has been achieved the patient should stop bearing down, and breathe deeply as she is anaesthetized. Delivery should never be attempted when the patient is semi-anaesthetized as she may suddenly strain, force the inadequately controlled head through the vaginal orifice and lacerate the perineum unnecessarily. With full anaesthesia, when the power of a contraction is waning or spent and control of the head is most complete, extension may be initiated by forward displacement of the brow and later of the upper jaw and sometimes the chin, by manipulation through the perineum by the fingers of the left hand, the vertex still being steadied by the right hand as the frontal region slowly passes over

the posterior labial commissure. The right hand is now rotated on the foetal head until the temples can be grasped transversely and the head is slowly and deliberately extended by drawing forward the bi-temporal diameter, the perineal skin, now under reduced tension, being grasped laterally and drawn forwards and towards the mid-line by the fingers and thumb of the left hand as the irregular face is freed from the posterior labial commissure, to minimize the risk of tearing or extending a laceration of the perineum. The perineum must not be drawn back over the extending brow and face as this would increase tension and the risk of laceration. When necessary an assistant may aid the birth of the head by pressing on the foetal breech through the uterine fundus. Finally a finger is passed behind one angle of the jaw and swept under the chin to the other side to free the mandible and complete the delivery of the head.

If the size of the vaginal outlet is inadequate for the passage of the foetal head during the second stage of labour or laceration of the perineum and posterior vaginal wall is imminent, one or more of the following signs may be evident:

- 1 Arrested progress of the 2nd stage of labour with the head resting on the perineum in spite of powerful uterine contractions and good co-operation on the part of the patient.

- 2 Depression of the perineum is not accompanied by dilatation of the vaginal orifice and the sub-pubic angle is acute.

- 3 Formation of a firm indistensible ring within the vaginal orifice.

- 4 Laceration of the lower third of the posterior vaginal wall before the perineum is fully expanded.

- 5 Blanching of the perineum as the head descends during uterine contractions.

- 6 "Beading" of the perineal skin with serum.

7 The appearance of multiple minute perineal fissures which tend to bleed

8 Progressive enlargement of a secondary caput succedaneum on the foetal scalp at the vaginal orifice

If such a state arises there are five possible courses open to the attendant. Labour may be allowed to proceed and the perineum to rupture, its extent being modified only by the skilful and correct control of the foetal head during delivery, an attempt may be made to limit extension of the laceration by pressure on a broad area of perineum, by inserting perineal sutures under graduated tension (Wright) or by a deep transverse incision of the perineal body (Howat), or the laceration may be forestalled by deliberate incision of the perineum. The first two courses involve a considerable risk of severe perineal laceration and foetal intra-cranial trauma and the third may cause perineal mutilation through stitches "cutting out," may damage the foetal face during delivery and, if used for subsequent reconstitution of the perineum as originally recommended, will not effect a satisfactory repair. Transverse incision of the perineum intended to prevent spread of a commencing perineal tear is a method of treatment which, although it is based on sound arguments and may, in a number of cases, limit the spread of laceration, has important disadvantages. Spontaneous rupture of a resistant perineum carries a significant risk of intra-cranial injury to the foetus, a laceration once started extends rapidly and may have spread too far before the check incision can be made, the hands at this stage are fully occupied in controlling the movements of the foetal head, especially as the resistance to its descent is suddenly removed by perineal rupture, and therefore the time cannot be considered opportune for a cautious and careful transverse incision of a body which has neighbours of conse-

quence. Further, in favourable cases a deep T-shaped wound involving the full thickness of the perineal body, including the superficial perineal muscles and anterior retractile fibres of the pubo-rectalis is difficult to repair efficiently and, if extension does occur, the difficulty is increased by the formation of a deep stellate lacinate wound. None of these methods afford any protection to the anterior vaginal wall or the subjacent urethral sphincters, and labour is unnecessarily prolonged.

When the laceration is inevitable or the advance of the foetal head is delayed by rigidity of the vaginal orifice, deliberate division of the perineum with scissors, if performed with prudence, will prevent unnecessary suffering by shortening the 2nd stage of labour, will minimize the risk of overstretching or tearing of the anterior vaginal wall, the muscular contents of the urogenital diaphragm, the anal sphincter and canal, and the rectal fascia and wall and will lower the forceps rate. It will also facilitate subsequent perineal repair by leaving a clear-cut surgical incision in a preselected position instead of an irregular lacinate wound and will reduce the hazard of intra-cranial trauma. This operation of episiotomy, referred to by von Oettingen as active protection of the perineum, should be delayed whenever practicable until the perineum is under tension so that the deeper structures will be displaced from the line of the incision. The patient should be lightly anaesthetized unless a local anaesthetic has previously been injected.

If the head cannot be fixed in its position of maximal descent by the fingers opposed to the ano-coccygeal region assisted by pressure on the uterine fundus, the perineum should be stretched laterally and firmly depressed by the separated index and second fingers of the left hand introduced into the vagina while the incision is being made. This digital stretching must,

however, be considered inferior to expansion by the advancing foetal head

The choice of incision is of considerable importance. A lateral incision gives little increase in available space, there is some possibility of inflicting damage on branches of the internal pudental artery, and unequal retraction of the wound edges with deep recoil of the divided levator fibres renders apposition and repair difficult. A median, posterior incision gives a maximal increase in available space with little irreparable damage to underlying structures, straightforward repair with a minimal amount of tension on wound edges and satisfactory healing in nearly all cases, its only disadvantage being the risk of laceration of the anal sphincters and canal if extension occurs. This risk may be obviated by converting it into an L-shaped incision, the lower limb of which passes through the tissues antero-lateral to the anal sphincter. Such an incision will divide the skin, subcutaneous tissue, superficial transverse perineal and bulbo-cavernosus muscles, the urogenital diaphragm and deep transverse perineal muscles, a few anterior fibres of the pubo-rectalis and the lower part of the posterior vaginal wall. The anal sphincters and canal, and the rectal fascia and wall are undamaged. The postero-lateral incision is intermediate in advantage and disadvantage between the posterior and lateral incisions. Bilateral postero-lateral incisions are to be condemned as the increase in available space at the vaginal outlet is no greater than that obtained by a single posterior incision, while the centre flap retracts, is difficult to suture in position and, after repair, usually forms an atrophic, inefficient perineum consisting of little more than vaginal mucosa and perineal skin. A timely episiotomy, if properly performed and efficiently sutured, will therefore conserve the integrity of the maternal tissues, assist involution of the

lower birth canal, prevent disorders of micturition and defaecation, and reduce the risk of traumatic intra-cranial lesions in the child, especially when premature. Overzealous care of the perineum at the expense of the anterior vaginal wall and apparatus concerned with urinary control is to be deprecated.

After episiotomy the foetal head should be delivered with care to prevent extension of the wound, special attention being directed to the completion of internal rotation, the maintenance of adequate flexion until the occiput is born, the displacement of the vestibule to the nape of the neck before secondary extension is permitted, and slow delivery of the head. Forceps delivery is necessary in only a small proportion of cases after episiotomy. It is occasionally permissible to give an intramuscular injection not exceeding $2\frac{1}{2}$ units of posterior pituitary extract after episiotomy if uterine contractions are feeble but not spasmodic, labour has not been prolonged, the membranes have not been ruptured for more than 3 hours, internal rotation is complete, an area of foetal scalp not less than 2 inches in diameter shows at the vulva during uterine contractions, the pubic angle is obtuse and there is no disproportion between the foetal head and the maternal bony and soft tissues. This treatment is unjustifiable when there is disproportion even of minor degree, when the membranes have been ruptured for some hours and spasmodic uterine contraction or contraction ring may be present, and when the vertex does not adequately expand the perineum during contractions.

In conclusion it should be stressed that every effort should be made to encourage the mechanism of delivery least liable to damage mother and child, meddling midwifery should be deprecated but conservatism should not be construed to mean inaction, and a decision as to whether any

particular line of treatment should be labelled conservative or impetuous should be based upon the after-history and findings at postnatal examination rather than upon a consideration of immediate technique. The importance of postnatal examination as a means of assessing results cannot be overstressed.

The majority of my illustrative diagrams have been drawn by Dr M Anderson, to whom I express my appreciation and thanks. Assistance with the translation of papers in foreign journals has been kindly given by Dr A Philipp.

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A Further Study of the Clinical and Pathological Properties of Malignancy

BY

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IN 1941 there appeared in the *American Journal of Gynecology and Obstetrics* (Vol xlii, 210-220) a paper entitled "Ovarian Malignancy." In it, the opinion was propounded that malignancy, of whatsoever kind, is a disease in which a single cell of the body, in favourable circumstances, begins to proliferate under a certain, internal stimulus and, by its multiplication, its daughter cells develop into a local growth, that all the cells of that growth, whether near or remote, are descendants of that parent cell, and that the malignant stimulus might affect two or more cells of different function and morphology somewhat simultaneously in different parts of the body.

The truth of those statements, I felt at the time, needed further factual elucidation. Let us deal with these clauses seriatim, first, the theory of the single cell proliferation.

It has been my good fortune, in the course of routine microscopy, to stumble upon several cases of extremely early malignancy of the female genital tract. One of these was found in the endometrium, 7 in the cervical canal, and 1 in the medulla of the ovary. The endometrial malignancy was clinically unsuspected, of course. It involved a microscopic part of the mucosa and extended in a cylinder-fashion from the surface down two-thirds of the depth of the mucosa. If one can judge of malignancy by the microscope, then this was malignancy. It was clean-cut, with sharply defined margins from the normal mucosa on either side of it, and there was

not a sign of papillary outgrowth in the surface, or of circumstantial reaction. At the margin of the growth malignant cells, clearly defined by a different protoplasm and different nuclear arrangement, lay side by side with normal endometrial cells. These latter seemed to be quite unconscious of an enemy in their midst. There was not the slightest sign of transition from the normal to the malignant type. The change was abrupt and clean, but the internal milieu of these two cells was as different as the characters of a peaceful citizen and a gangster.

In the early carcinoma of the cervix, the same seemingly inoffensive beginning of malignant newgrowth also was found. Here, however, there were certain enlightening discoveries. Not only was the growth clearly delineated from the normal cells, but certain glandular tubules, cut transversely, showed malignant cells affecting only a segment of the lining epithelium, while the rest of the circumference was lined by normal cervical mucosa cells. This delineation in minute ducts was found very frequently, and in them there was not a vestige of transition from one type of cell to the other. I have found that transitional types occur only when inflammatory reaction disturbs both types—the malignant and the non-malignant cells. The margins in the specimens were as clear-cut as social distinctions. Here in this region, where the chief function of the lining cervical mucosa would seem to be to secrete a downward flow of thick quasi-impervious mucus to protect the uterine mucosa from invasion,

it was noticeable that the malignant cells were devoid of that chief function, and this cell energizing seemed to spend itself, not in functional activity, but wholly in division. We can assume that, as the body is the composite picture of all its component cells and as the human body is limited to the energy it can expend at any given time, that energy can dispel itself in any one way to its full capacity, but not in more than one way to that same degree. So it would seem that division and function are maintained in an inverse ratio. It is generally conceded that when a normal cell is in a state of division, its chief normal function is temporarily abrogated, not only until the division has been completed, but also until the newly-born daughter-cells have grown to a state to initiate their own function. Then function goes on in a crescendo until full maturity requires reproduction to renew the youth of the cell. Malignant cells never seem to reach maturity before division again interrupts development. The same rules apply to the individual. It is conceded, and has been frequently expressed in literature, that the normal woman's cerebral creative ability is abrogated during pregnancy. It has been stated that a woman in her pregnant state has never produced anything noteworthy, other than a child. And, like cells after karyokinesis, the child's functions during intrauterine aquatic life and in the terrestrial stages of living are in a state of progressive functional capacity until maturity. So it would seem that the inference is justifiable that the highest functions of cells are first lost in malignancy and that this deprivation of function is progressive until all cell energy is consumed in a speed-up of cell division.

The microscopic newgrowth in the ovary was, of course, discovered only at biopsy. It was exceptionally small microscopically, as stated above, and was a malignant

papilliferous growth. It undoubtedly was malignant from its inception, because it was malignant throughout. What the structure was, in which the growth took its origin, could not be determined.

All the above-quoted cases show quite clearly that malignancy has something which other non-malignant cells do not possess, and that that property of heightened cell-division is transmissible from cell to cell only through parent cell to daughter cells, and not by propinquity or even contiguity, for we have seen that seemingly normal cells, so far as we can judge by morphology and staining properties, can carry on normally, while juxtaposed against cells presenting all the hall-marks of malignancy. If this be true, then the clinical inference is clear-cut, that though certain tumours of the ovary may be looked upon as being prone to malignancy, yet we must conclude that those tumours are malignant or benign from their inception, and if a large ovarian tumour is benign in its greater mass, and shows malignancy at one spot, that malignancy is an accidental after-development brought about by a new chain of circumstances which has affected one or more susceptible cells.

These mixed types of ovarian tumours are preponderantly of the pseudomucinous types, which are now looked upon as teratoid tumours, in which the endoblastic element is the dominant type of growth, and the reason why this form of ovarian newgrowth is prone to carcinomatous development (not change) lies probably in the fact that endoblastic carcinomatous growths greatly outnumber ectoblastic epithelial cancers. The carcinomatous types arise chiefly in columnar epithelial surfaces and areas covered by so-called transitional epithelium. These are the easily vulnerable internal surfaces of the body, compared with the imbricated

epithelial coverings of the body's exterior. For that same reason teratoid tumours and teratomata of the ovary are prone to heightened division to the state which we designate as malignant.

Malignancy, however, both clinically and pathologically is a purely relative term. But what exactly do we mean by that statement? It admits of several interpretations. There are tumours which clinically are malignant, but by microscopic criteria are benign, and the reverse is equally true. That there are no hall-marks whereby pathologists can distinguish between malignancy and non-malignancy is shown by the fact that cautious pathologists nowadays will not venture a diagnosis without a knowledge of the clinical history. In other words, a prognosis from a pathologist, like that of a clinician, is based upon a review of the course of that and similar cases. Experience has taught caution in such cases, and experience is the main guide to the value of any such judgment.

The susceptibility of the patient is behind the progress of any malignant newgrowth. Local malignancy may be developed by the assistance of an abnormal local dysfunction, such as chronic infection or other trauma, in a patient who has no susceptibility in any other part of the body. In other words, the local trauma is the cause of the local development of malignancy. In many such cases the corporeal resistance may prevent any such newgrowth from implanting itself elsewhere in the body, until such time as corporeal cellular resistance is turned into cellular susceptibility. But more of this later.

I am decidedly of the opinion that, though local malignancy may develop through local adjuvants, the other parts of the body may not only be not susceptible to invasion, but may be decidedly inimical to it. Such are the cases, which, when the malignancy is locally eradicated by what-

soever means, become permanent cures and, *per contra*, trauma may initiate a local newgrowth in a resistant tissue where other organic areas are more susceptible. In these cases the metastases may outgrow the primary focus. In this respect malignancy follows closely the rules that govern infection, except that the mortality following malignant invasion is higher, owing to the lack of progressive immunity such as is obtained under infections. Herein lies the great difference between diffuse malignant invasion, and acute and chronic infections. In malignancy the chief trend seems to be towards a loss of any natural immunity, whereas in infections the toxæmia, in most cases, seems to heighten defence.

A STUDY OF METASTASIZING

Metastases from a malignant growth may reach remote areas by two distinct routes (1) by the lymphatic chain, and (2) by the blood-stream, or (3) by a combination of both. There is nothing new in that, of course. But we must ask ourselves, do all the cells which detach themselves from the primary growth survive in their new environment? Or, if not, do they all perish? Or, if not, can they be dormant for years in uncongenial surroundings to light into activity when more favourable circumstances develop? And, if so, have we any knowledge of the length of time such dormant potentiality may continue? As pointed out above, local susceptibility due to trauma may develop when clinical evidence as gathered from the course of the disease points to a general corporeal immunity. In such circumstances the local invasion may remain local for an indefinite period and local eradication then usually portends a cure. On the other hand, local and corporeal susceptibilities may be found in various degrees and, therefore, the local

manifestation may vary in all degrees of extension in comparison with the metastatic growths. In many instances the remote metastases may so dominate the clinical picture that the primary invasion remains insignificant and may be completely overlooked. The same conditions obtain in infections, to the degree that the parallel is almost, but not quite, perfect.

As regards the development of metastases, can we form any conception of their *modus operandi*? From a study of clinical cases of malignancy, several hypotheses immediately present themselves for consideration.

Do malignant cells from a newgrowth escape in showers into the circulation? Is it a matter of indifference whether it be direct into the blood-stream or through the intermediary lymphatic chain? Or does only an occasional malignant cell detach itself and invade the system? Here again a parallel is found in blood-stream infections.

But as regards malignancy the much more important question follows naturally upon the above: what happens to these blood-stream invasions? Do they survive for years in the blood-stream, or is the circulation freed from them? If the blood-stream is soon cleared of these cells, what happens to them? Are they digested in the blood-stream or do they become localized? And if localized in the tissues, are they destroyed immediately or may they remain in a state of suspended animation, to revive in more favourable circumstances? Let us see what clinical evidence we can bring to bear upon these questions.

Let us study a few enlightening cases.

I. A case of chorionepithelioma. We know that chorionepithelioma is a malignancy of syncytial and Langan's cells. We know also that throughout the stages of normal placental development these

cells invade the maternal blood-stream in large numbers, causing emboli in liver, spleen, brain, and so on. Yet eventually they are all liquidated by the enzymotic action of the body liquids. Occasionally, however, under the stimulus of an abnormal endocrine agency, they get the upper hand and the most malignant type of newgrowth develops. Some years ago, I confined a primipara. Judging in retrospect, everything about her labour and recovery was as normal as could be. Eight months later she went to her physician complaining of severe pains in her bones. This had come on suddenly within the past 2 weeks. X-rays showed her vertebrae and long bones riddled with newgrowth. The lungs were widely invaded also, and metastatic newgrowth of the chorionepitheliomatous type was suspected. Examination revealed a normal pelvis with a normal involuted uterus. Menstruation since delivery had been regular and normal. She died after a short illness and the diagnosis of chorion epithelioma was confirmed. Gross and microscopic examination of the uterine wall showed not a trace of newgrowth there, nor any other distinguishable primary growth from which these metastases had proceeded.

Were some, or even one, of the usual normal placental blood invasions not destroyed during those intervening 8 months? If we concede this, they must have remained in a dormant potential state during a great part of that period, only to break down the natural body immunity by their excretions, finally to establish a comparative symbiosis and an eventual ascendancy. There comes considerable elucidation of this difficult and occult subject from two different types of cases of fairly recent date. In my monograph on "Endometriosis" (now in the press) are details of 2 cases of stromatous endometriosis with malignant properties. Both these cases

were followed over a period of 10 and 12 years respectively. Endometriosis is a disease that is restricted to the organs which lie in the pelvic region. The exceptions to the rule are so few as to be curiosities. I laid emphasis upon the fact that the susceptibility of the pelvic tissues is due to their propinquity to the source of the ovarian secretions. The nearer the structures to this source, the greater their susceptibility to implantations of endometrial ectopic cells. We have in this a very pronounced selectivity of endometrial cells for a certain specific, chemically impregnated tissue. I have maintained for years that selectivity, be it either bacterial or cellular, is the basis of disease specificity. The underlying cause of this selectivity or susceptibility is undoubtedly biochemical, be it endocrinological or metabolic, whether these be hereditary or acquired.

In these 2 malignant endometriotic cases, though the ovaries had been removed upon discovery of the disease, and though each had had repeated series of deep X-rays, nevertheless the spread of the disease in the pelvic structures continued with remissions over a period of 10 and 12 years. The long periods of remissions were due to the stunting effect of ovarian ablation and to the stunning effect of the X-ray treatments. In spite of these two factors which are usually curative these cells not only were able to survive the ablation of the ovaries, but became so inured to X-rays that they became X-ray fast.

Roentgenograms of the whole body of one of these cases immediately following death were negative, and gross examination at autopsy did not show any evidence of metastases outside the pelvic region, yet the microscopic studies of the lungs revealed lesions of small metastases throughout the lungs. The second case, upon which I could not secure an autopsy, was X-rayed one month before death and the lungs did

not show anything abnormal, yet another picture taken just before death revealed the lungs in a state of 'snow-storm' from thousands of metastatic growths resembling a miliary tuberculosis. It would seem that certain clear inferences may be drawn from these cases. The susceptibility of the pelvic tissues and the non-susceptibility of the extrapelvic areas to the newgrowth was maintained throughout 10 and 12 years, until such time (death was due to uremia from ureteral obstruction in both cases) as the tissue individualistic characters were submerged in the poisons which flooded the system, making the extrapelvic tissues susceptible just before death. It also tends to confirm the opinion that the malignant cells may increase in hardihood owing to any prolonged resistance that they may have to overcome, and that as body resistance, which means tissue specialization, is lost all are subdued to the malignant invader.

But there is a deeper lesson to be learned from these 2 cases. I doubt if anyone could maintain that malignant cells got free in the circulation only when the extrapelvic susceptibility was established, and that in that last month of life the body was flooded with millions of dispersed cells. Rather must one infer that throughout these 10 and 12 years malignant cells invaded the blood-stream just as do bacteria in pyaemia, but that, owing to the uncongenial surroundings, they were overcome and destroyed, and that the survival of the malignant cells of this continued blood-stream invasion was possible only when biological tissue differentiation was lost in the last months of life. In these cases, as distinguished from the case of chorionepithelioma cited above, there was always a primary source in the pelvis to supply the seeds. In the case of chorionepithelioma such a primary source could not be found in the uterus. The inference here must be that

there must have been a potential dormant nidus (dormant for 8 months after delivery) somewhere in the body, not necessarily in the uterus, though this be the common-site of such chorionic activity

Another recent case is of special interest. A patient, 37 years of age, had a radical breast operation for a small malignant tumour. This was immediately followed by a series of deep X-ray treatments. Fifteen months later she complained of flashes of light in one eye. Wasserman and tuberculin tests proved negative. Roentgenograms of the whole body were negative at that time. Three months later the other eye became similarly involved and total blindness followed. X-ray examination of the bones of the body again proved negative. Six months later she complained of severe pain in the back. X-ray examination now revealed a metastatic involvement of two vertebrae and two ribs. The symptoms have grown progressively worse, due to continued anorexia, nausea and gradually increasing cachexia.

Here is a case in which selectivity of cells has reached a high degree. The inference, I think, is here again justified that malignant cells which reach the circulation are for a long time destroyed, but that eventually, by their destruction, a progressive symbiotic chemical balance is established first in one tissue, then in another, eventuating in a generalized corporeal susceptibility. I think the contention cannot be maintained, as is frequently held, that all aberrant malignant cells are destructive. On the contrary, their power to localize and flourish is dependent upon corporeal and organic resistance which, however, usually gives way slowly under the repeated and increasing invasions. Special organs, or parts of organs will differ in the time and the degree of their tolerance of the invasion, which will explain how one special tissue, such as two choroids in my case,

became the first organs to yield to the flood.

Comparing the size and singleness of the optic artery with the blood-vessels of the rest of the body, it is estimated that a single malignant cell which had escaped and reached the circulation would have to complete the round of the circulation from 1 to 10,000 times before chance landed it in a single choroid, and this chance of a single cell would have to be repeated before the other choroid was attained. In this case 3 months elapsed. This case is a striking example of specificity of new-growth cells for certain definite, restricted areas of favourable biochemical composition. We are forced to the conclusion that invasions of the blood-stream are frequent and progressively copious, but that few of these survive the freedom of the circulation or the stasis of inimical organs. Any susceptible tissue, though the first to be involved with metastases, may be surpassed and overshadowed later by the rapidity of other metastatic growths. It is quite evident that different tissues may lose their immunity quickly to newgrowth, but to a lesser degree than other tissues that have resisted longer, but the defence of which, when once overcome, collapses to a more profound degree. That is evidenced in these quoted cases by the longer resistance of the bones, but finally, when their resistance was broken, the newgrowth flourished like the proverbial bay tree. So the stages of metastasizing would seem to be destruction, inimical tolerance, pacific symbiosis, and lastly, surrender to the uninvited guest.

The concept that floods of malignant cells are constantly invading the blood-stream, and localize and thrive only where the soil is favourable, carries with it the explanation for the frequent bilaterality of metastases in similar bilateral organs. For example, the constant bilateral invasion of the ovaries in Krukenberg's tumours,

the involvement of both ovaries in malignant papillary growths, the frequent involvement of both breasts in malignancy, the involvement of many vertebrae before other bones are involved in metastases from breast malignancy, the contamination of the choroids of both eyes before any other parts of the body were affected, in the case cited above

But aside from the corporeal resistance of special organs there are factors inherent in the malignant cells themselves which determine to a certain degree the frequency and numbers of cells set free in the circulation. There are two commonly known characters and doubtless many other less understood. These are (1) the size of the malignant cells, and (2) the character of the supporting tissue about the malignancy.

In these respects malignancy resembles infections. The larger organisms of infection, such as syphilis, for example, take a long time before reaching the general circulation, and if the primary focus of infection can be eradicated, the septicæmic stage may be avoided. The spirochaete is at one extremity of size differentiation. At the other extremity are the ultramicroscopic organisms of virus diseases which reach the circulation almost directly.

The more rapidly a malignant cell multiplies the smaller and more embryonic will be its progeny and, therefore, the quicker it will invade the lymphatic and blood-stream.

On the other hand, the degree of succulence and vascularity of the matrix primarily invaded will determine the facility with which malignant cells may escape into the lymph or blood-streams.

All these are chiefly mechanical factors quite apart from the biochemical adjuvants and inhibitors, inherent or developed in the liquid and semi-solid tissues of the body.

Malignancy is commonly a tissue disease, that is, its growth and its metastases settle in semi-fluid tissues, but leucaemia, which is a malignancy of free cells, finds its habitat in its normal site—the blood.

CONCLUSIONS

Malignancy, to the clinician and pathologist, is a relative term. In the vast majority of malignant cases aberrant malignant cells are constantly invading the blood-stream. These are usually rendered impotent for various periods by the body fluids, or cells. The common concept that malignant cells are not destroyed, but remain long in the circulation, is not sustained by a careful study of clinical cases. Local territorial cancer is usually primarily met by a resistance outside that territoriality. This extra-territorial immunity or lack of it, determines the slowness or rapidity of the metastasizing process.

Tissues differ in the time and the degree of yielding their immunity to the invading cells. Under the influence of repeated invasions a tolerance between the host's tissues and the uninvited guest is eventually established to the ultimate destruction of the patient. Frequent blood invasions and the similarity in biochemistry of bilateral organs and the predilection of certain types of malignant cells for that environment determines the simultaneous bilateral incidence of metastases in those organs.

Lord Rutherford stated that atoms behaved as if they were endowed with intelligence. I have repeatedly asserted that the selectivity of microbes for certain tissues is the specific property which gives diseases their diagnostic characters. Cancer cells possess this selectivity to a higher degree than microbes, and it determines their clinical courses.

A Case of Obstructed Labour due to Dysgerminoma

BY

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THE patient, Mrs S , a primipara aged 22 years, was transferred from the Radcliffe Infirmary Maternity Home to my ward on March 9th, 1937, as a case of obstructed labour

She had been attended by a midwife in the country and had been, I believe, in labour for 48 hours before she was seen by a doctor, who immediately sent her into hospital

History of pregnancy

There was no abnormality and labour began at the expected time

On admission to the Maternity Department she was found to be much exhausted, the head was above the brim and the os undilated. The foetal heart could not be heard. A firm mass could be felt in the pelvis which appeared to be preventing the descent of the head. After treatment and rest her condition improved and as no advance was made in spite of good pains I was asked to see her, with a view to Caesarean section

On examination

The patient was a small but well-developed woman, tired and worn out. The uterus was contracting well but the head could not be pushed into the pelvic inlet and there was marked over-riding. The foetal heart could not be heard.

I found a very curious tumour in the pelvis, it lay behind the lower segment of the uterus and felt like the lower segment of a large bun, jammed between the head and the sacrum. Its surface was almost

smooth and it was firm and solid—not cystic—in consistence. It appeared to be about 5 inches in diameter and much flattened from before backwards. It was presumably an ovarian tumour but of a type with which I was unfamiliar.

Operation As the condition of the patient had now improved I opened the abdomen and removed a dead male child through a low vertical uterine incision which I covered with the bladder reflection of the peritoneum.

The tumour was seen to have the size and shape ascribed to it and to be a growth of the right ovary but as the patient's condition was none too good an attempt was not made to remove it and the abdomen was closed.

Convalescence was complicated by a streptococcal urinary infection which, however, soon yielded to treatment.

On July 1st, 1937, the patient reported that she was suffering from menorrhagia, but was otherwise in good health.

On July 13th, 1937 I operated again and found the tumour rather larger than before and adherent to the structures in its neighbourhood. The adhesions were separated without difficulty and the tumour removed. As it did not appear to be a malignant growth I did not perform a pan-hysterectomy. The patient made an uneventful convalescence and was discharged on August 7th, 1937.

I saw the patient last on March 21st, 1942. She is in excellent health. Her weight is satisfactory, she looks well and she has

no complaints except, recently, occasional menorrhagia

On examination there is no pelvic, abdominal or other abnormality

For the pathological report and review of the literature of these rare tumours I am indebted to Dr Robb Smith, Director of Pathology, the Radcliffe Infirmary, Oxford

PATHOLOGY

The specimen consisted of a whitish oval tumour weighing, when fixed, 910 grm and measuring $14.5 \times 12 \times 8$ cm. The surface was irregularly lobulated, at one point the Fallopian tube could be recognized and appeared natural. The cut surface was of a uniform cream colour in which ran bands of translucent material, and at the centre there appeared to be some liquefaction. It was everywhere encapsulated.

Histology (R I S H 63193)

The tumour consists of collections of large round cells arranged in columns or masses lying in a fibrocellular stroma.

The tumour cell is oval, measuring (in paraffin section) 15×12 with a nucleus 12×10 . The cell membrane is indistinct and the cytoplasm is faintly eosinophil and finely granular. The nucleus is round to oval with a dense nuclear membrane. There is a solitary prominent nucleolus. The nucleus is rich in basic chromata which is arranged in the form of nodes with fine threads joining them. The nucleoplasm is colourless. Binucleate forms are frequent and numerous cells show karyokinesis.

The supporting stroma divides the collections of cells into columns or islands. This stroma is profuse and consists of collagen and reticulin fibrils in which are lying fibrocytes and reticulum cells. A striking feature is the large number of small lymphocytes and histiocytes in the stroma,

and many of the latter have formed giant cells. This cellularity of the stroma is most marked in the region of the blood vessels and in some places the histiocytic giant cells and lymphocytes recall a 'tubercle' though there is no necrosis or caseation. There are no strands of reticulin between the tumour masses. The tumour is not highly vascular and there are numerous areas of degeneration probably due to this fact. There is very little fat in the tumour and it chiefly occurs in the histiocytic giant cells. Normal ovarian tissues could not be made out.

HISTOGENESIS

This type of tumour occurs in both sexes, though there are striking differences in age incidence (in females in the second and third decades, in males after the fourth decade) and in prognosis (in females it is almost invariably benign, in males highly malignant, though Payne¹ has shown that the prognosis is better than is generally thought). Its relation to the gonadal tissue was first recognized in those occurring in males and Chevassu² suggested that they should be called 'seminome'. Similar tumours were frequently found in cryptorchids and Peyron³ described the ovarian form of tumour, suggesting that they were derived from the medullary cords which had differentiated towards male elements.

However, the matter was classified by Meyer⁴ who proposed the name dysgerminoma and suggested that they were derived from cells of the germinal epithelium which have not been determined to cells of either male or female type. This is in keeping with the observations that they frequently occur in hermaphrodites or persons with poorly developed genitalia and that they do not show any evidence of hormonal activity.

The general view is that these tumours in the female are essentially benign though

Wolfe and Kaminester," and Doubniet* have described cases with definite evidence of malignancy and the former authors regard the prognosis as poor

Portions of the specimen are preserved in the museums at the Radcliffe Infirmary, Oxford, and St Bartholomew's Hospital, London

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DYSGERMINOMA

- Fig 1 The surface of the tumour (natural size)
 Fig 2 The cut surface of the tumour
 Fig 3 Showing the general structure of the tumour $\times 100$
 Fig 4 Showing histiocytic giant cell $\times 210$
 Fig 5 Showing the character of the tumour cells $\times 440$



FIG 1

D A A



FIG 2

D A A

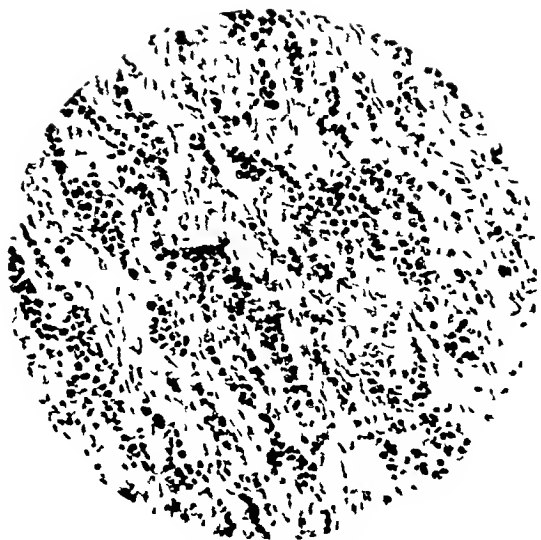


FIG 3



FIG 4



FIG 5

A Case of Full-time Hydatidiform Mole with Central Placenta Praevia

BY

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THE following case of hydatidiform mole shows some interesting features

CASE HISTORY

Mrs O'D, an Irishwoman, aged 32 years, was admitted as an emergency case of antepartum haemorrhage to the maternity wards, Dundee Royal Infirmary, on June 21st, 1941. She had had 2 normal confinements in 1932 and 1939 respectively, and a 2 months' miscarriage in July, 1940. Her menstrual periods had always been regular, the last one being on September 26th, 1940. She had not booked with her doctor until late on in her pregnancy, but her blood-pressure and urine were normal at each visit thereafter and her general health was good. Breast enlargement took place as usual, and supposed foetal movements were felt right up to the day of admission, though less than with previous pregnancies. Growth of the abdomen was progressive throughout the pregnancy though the patient thought her abdomen was unusually large. There was not any bleeding or discharge until the fortnight before admission, when a brown discharge was present intermittently, neither was there any visual or urinary disturbance. Oedema of the feet appeared during the last 2 weeks and increased in the 4 days before admission.

On rising from bed on the morning of June 21st there was a sudden painless flood of blood on the floor. The patient

went back to bed and the bleeding stopped. The doctor was summoned, and on his arrival there was further bleeding. Backache was now being felt. A vaginal examination revealed a boggy mass over the internal os, which was one finger dilated. The patient was sent into hospital with a diagnosis of placenta praevia.

On admission she was seen to be a well-nourished woman with fairly good colour but rather a toxic appearance. Gross oedema was present in the lower limbs and slight oedema in the lower part of the abdominal wall. There was not any noticeable oedema in hands or face. The blood-pressure was 180/120 and the urine contained albumin. The temperature was 97.4°F, pulse-rate 88, and respiration-rate 20. She complained of backache but not of abdominal pain. There was not any fresh haemorrhage, though traces of previous bleeding were seen about the vulva. The abdomen was the size of an exceptionally large full-time pregnancy, and had the firm feeling associated with a partially-concealed accidental haemorrhage. Foetal heart sounds were not heard and foetal parts could not be palpated. A diagnosis of probable accidental haemorrhage was made. She was given an injection of $\frac{1}{4}$ grain morphine sulphate and slept for an hour. The pulse-rate was watched, and remained steady at 88 per minute. When she woke up she complained again of backache, but there was not any further bleed-

ing Two hours after admission a vaginal examination was made without an anaesthetic. The cervical os was found to admit one finger but the cervix was hard and did not suggest that the patient was in labour. Placental tissue was felt covering the internal os. Bleeding did not occur during this examination, though some old blood was present in the vagina. Even with fundal pressure, by an assistant, foetal parts could not be felt through the placenta, and a diagnosis as to the presentation could not be made. In view of the central placenta praevia preparations were made for immediate Caesarean section.

OPERATION

The patient was anaesthetized with general ethyl chloride and ether. Even under the anaesthetic foetal parts could not be palpated. The abdomen was opened through a right paramedian incision extending above and below the umbilicus. The tissues appeared to be rather bloodless, so that bleeding in the abdominal wound was minimal. The uterus was normal in colour and appearance though unduly large. The abdominal cavity was packed off and the classical operation was performed. An enormous vesicular mole was found to be filling the uterine cavity. It was removed in handfuls, vesicles and fluid being ladled out into buckets on the floor. The mole came away very easily, and appeared to have only slender attachments to the uterine wall. There was scarcely any bleeding during the removal of the mole, and the uterus contracted well. The placenta was found to be covering the lower uterine segment as a complete central placenta praevia, and was stripped off by hand. It was more firmly attached than normally to the uterine wall, and some bleeding occurred during its separation. The uterus then contracted down and appeared

to be empty apart from some blood and detached vesicles. There was not any sign of infiltration of the uterine wall by the mole, and the organ looked healthy inside and out. Hysterectomy, therefore, did not appear to be indicated. Pituitrin was injected into the uterine wall to maintain contraction and retraction and the incision was sutured. In spite of the abdominal packs vesicles had been spilled into the peritoneal cavity, these were removed so far as possible, though some inevitably must have been left behind. Unfortunately note was not made of the state of the ovaries, though had any gross enlargement or cystic condition been present it would almost certainly have been noticed during the clearing up of the pouch of Douglas. The abdomen was closed. The patient's general condition at the end of the operation was satisfactory. Her pulse was of good quality and the rate 104 per minute, and the uterus was well contracted. Some vesicles and blood were found to have been passed *per vaginam* during the operation.

SPECIMEN

The hydatidiform mole was composed of vesicles varying in size from tiny ones to those the size of large raisins. Much fluid had also been evacuated from the uterus as though the vesicles were bathed in it. There was not any sign of a foetus or umbilical cord or amniotic sac. The placenta had a normal surface area for a full-time pregnancy but was a good deal thinner than usual, was not divided into cotyledons, and merged indefinitely at the edges into ill-defined membranous tissue from which the vesicles arose. It looked as if the chorionic space had been obliterated, and the vesicles appeared to be attached to the upper or foetal surface of the placenta. Blood-vessels were not

present on the surface of the placenta. Microscopical examination of a piece of placental tissue showed it to have a rather dense, fibrous structure. The villi showed hydatidiform degeneration with absence of vessels, but there was little or no proliferation of the trophoblastic epithelium on their surface.

PUERPERIUM

On the day after operation the temperature rose to 105.4°F , and the pulse-rate to 130. The patient was extremely hot and dry and slightly delirious. The blood-pressure was 120/65 and the urine did not contain any pus cells. The abdomen was soft, but a few scattered rhonchi were present in the chest. The pyrexia did not appear to be associated with sepsis but rather to be of the nature of a heat-stroke, the day being exceptionally hot. Another possibility was that the hyper-pyrexia was of an anaphylactic nature resulting from absorption of toxic fluid by the opened-up uterine sinuses during the operation, or even, perhaps, from the presence of the stray vesicles in the peritoneal cavity. The treatment given was ice-bags to the head, Dover's powder, and sulphonamide as a precaution. The next day the patient was better, the temperature falling to 103.4°F and the pulse-rate to 110. She was taking fluids well, was passing urine normally and did not have any complaints. The blood-pressure was 110/62, and the urine contained only a trace of albumin. The temperature fell by lysis, reaching 98.8°F on the 4th day. There was another sharp rise to 103°F on the fifth evening without any symptoms, falling to normal in 24 hours and remaining normal for the remainder of her stay in hospital.

Engorgement of the breasts was appearing by the 3rd day with consequent discomfort, a course of stilboestrol tablets was,

therefore, given over a few days and successfully inhibited lactation. The lochia were normal apart from containing vesicles for 24 hours after the operation. By the 6th day, as she was looking rather pale and her haemoglobin was only 50 per cent, a blood examination was made and excluded any serious blood disease. A transfusion of 1 pint of citrated blood was given on the 7th day, with general improvement. Thereafter 30 grains of ferr et ammon cit was given 3 times daily. The abdominal incision healed normally. Albuminuria disappeared after the 7th day, and the blood-pressure remained steady at about 130/80. She was allowed up on the 16th day and discharged home in good health on the 21st day.

Specimens of urine submitted to the Pregnancy Diagnosis Laboratory, Edinburgh, for Aschheim-Zondek tests were taken 48 hours and 21 days after operation. The reports read "Positive, rather a weak reaction," and "Negative" respectively. The Wassermann reaction was also negative.

SUBSEQUENT HISTORY

The patient reported on October 13th, 1941, in good health. The Aschheim-Zondek test was negative. She had had a period lasting 6 days exactly 6 weeks after the operation, followed by another two periods lasting 4 days each at regular monthly intervals. Pelvic examination showed the uterus to be completely involutioned and lying anteriorly, the vaginal walls and cervix were normal and there was not any discharge. The abdomen was flat and did not show any abnormality. The blood-pressure was 134/80 and the urine clear of albumin. The haemoglobin was 106 per cent. The patient's only complaint was that her hair was falling out badly.

She reported again on April 4th, 1942, when the Aschheim-Zondek test was again negative, she was still well and her hair had grown in again. The patient, who now weighed over 12 stone, had put on 7 pounds since the operation. Menstrual periods were regular and normal each month. The blood-pressure and urine were normal. On June 25th she again reported well, and on August 6th the Aschheim-Zondek test was still negative.

DISCUSSION

It is generally agreed that the true hydatidiform mole as we know it clinically, without placenta or foetus, or at most with an imperfectly developed foetus, is the result of hydatidiform degeneration of the entire chorion in the early weeks of pregnancy before the placenta has had time to form. The mole continues to grow and is usually expelled some time in the first half of pregnancy. De Lee¹ states that the entire chorion is usually involved, but that either the chorion frondosum or chorion laeve may be alone affected. The ovum, he says, is primarily diseased. In the case I have recorded it would appear that the hydatidiform change affected the entire chorion and occurred not in the very early weeks but as the placenta was developing. The foetus presumably perished. Cases have been recorded in which a partial hydatidiform degeneration of the placenta has been recognized later in pregnancy, even with the birth of a live, normally-formed child. My case, in point of time of onset of the vesicular change in relation to the period of gestation, would appear to fit in between these two extremes.

Hertig and Edmonds,² in a series of 1027 spontaneously aborted ova, found that early hydatidiform changes could be shown microscopically in the villi of 40 per cent. In about half of the whole series the

ovum was "pathologic," i.e. defective or absent, and in the other half "non-pathologic" or normal. Hydatidiform degeneration however occurred about 6 times as frequently in the "pathologic" as in the "non-pathologic" group. The authors explained these changes in the villi, which they considered physiological rather than pathological, as follows. The foetal circulation should start functioning at about the 5th week of pregnancy. If the foetus is absent or defective the circulation cannot function. But the chorionic epithelium in contact with the maternal sinuses continues its normal activity, and fluid accumulates in the villi by absorption and/or secretion, as there is not a foetal circulation to carry it away. These investigators, like others, found that the classical hydatidiform mole is uncommon, and either is not associated with an embryo at all or rarely with a very defective one. They consider that the classical mole is derived from the earlier type described, which for some reason fails to abort at the usual time.

It must be very unusual to find a placenta associated with a hydatidiform mole, and even more extraordinary to find the placenta as a central placenta praevia. Why the placenta should have continued to grow long after the foetus presumably perished is difficult to understand, as it did not serve any physiological purpose. Its continued growth can only be considered pathological, as indeed the microscopical appearance of its structure confirms. Presumably the hydatidiform villi in the placenta went on expanding just as the rest of the mole grew, and the fibrous tissue formation suggests a defensive reaction on the part of the maternal organism.

I cannot find any record of a full-time hydatidiform mole in the literature, though references are made to cases which went to term or even over. De Lee saw only one case of vesicular mole which did not ter-

minate before the 6th month, and in that one the mole ceased growing and was expelled at term. He refers to cases of Depaul and Madden which went over term. Brews³ mentions 2 cases with amenorrhoea of over 40 weeks, and refers to a case of Blair-Bell's in which amenorrhoea of 10 months was associated with a carneous hydatidiform mole which enlarged the uterus to the size of a 12 weeks' pregnancy only. Brews, incidentally, points out that cases recorded in the literature of vesicular moles with an abnormally low or negative hormone assay are probably cases of "missed" abortion of the separated mole. This raises the question in one's mind whether some of the cases referred to in the literature as going to term, or over, were really just cases of "missed" vesicular molar abortion.

The absence of any antenatal hormone investigation in my case makes it difficult to say whether it was a case of "missed" abortion or not, but the enormous size of the mole, the steady increase in enlargement of the abdomen as noticed by the patient and the presence of a weakly positive Aschheim-Zondek test 48 hours after the evacuation of the uterus all suggest that the mole was still growing up to the time of its removal. The blood-stained discharge which occurred during the fortnight preceding admission to hospital, and the bleeding on the morning of admission, were obviously the result of a slight separation of part of the low-lying placenta.

Cases of hydatidiform degeneration of the placenta associated with a normal foetus have been observed by various writers. Ganner⁴ and Barnes⁵ have each published a case in which the condition was present with a central placenta praevia.

Toxaemia is often associated with a vesicular mole. Sherman⁶ found it to be present in 29.4 per cent of a series of 78 cases, and this seems to be about the usual

figure. In my case toxaemia was so well marked that it at once suggested a diagnosis of accidental haemorrhage rather than the correct diagnosis of placenta praevia which the patient's doctor had made by vaginal examination. The patient stated that she had felt foetal movements throughout the pregnancy. In view of the enormous bulk of the mole and associated fluid it might almost have been surprising if she had not felt movement of some sort inside her. An even more interesting phenomenon was Nature's effort to produce a milk supply for a foetus which presumably perished early in pregnancy.

At the operation there was not any penetration of the mole into the uterine wall. The Aschheim-Zondek reaction, which was only weakly positive 48 hours after evacuation of the uterus, did not suggest that the mole had been of an actively proliferating kind. One can only conjecture as to the fate of the stray vesicles left inside the abdomen, but probably they would soon perish. The subsequent negative Aschheim-Zondek tests up to 13 months after operation were very satisfactory, and suggest that chorionepithelioma will not develop.

It is generally agreed that, following hydatidiform mole, a period of time may elapse when the Aschheim-Zondek test is negative, even though chorionepithelioma may ultimately develop with a return of the positive reaction. Payne,⁷ in a study of the relevant literature, finds that the longest latent period recorded between the antecedent pregnancy and the development of chorionepithelioma, prolan tests being taken frequently and showing negative results, is 6 months. This author considers that after the first negative test following expulsion of a mole a follow-up of at least a year is necessary before the possibility of malignant degeneration can be ruled out. Mathieu⁸ on the other hand gives as his opinion that the Aschheim-Zondek test

cannot be negative in the presence of living chorionic tissue and that, following hydatidiform mole, the finding of 2 or 3 negative tests (sufficient to avoid the possibility of a laboratory error) means that chorionepithelioma will not develop

That normal pregnancies may follow vesicular mole is generally understood. There does not appear to be general agreement, however, as to whether there is a tendency to recurrence of the condition in subsequent pregnancies.

SUMMARY

1 A case of full-time hydatidiform mole without a foetus but with a central placenta praevia, and associated with severe toxæmia, is described

2 The treatment by Caesarean section in view of the central placenta praevia revealed the true condition

3 Interesting points about the puerperium such as hyper-pyrexia and the appearance of breast secretion are noted

4 A follow-up of 13 months showed persistently negative Aschheim-Zondek tests and a return to normal menstrual periodicity and good health

5 The absence of a similar case in the literature is noted

6 Points relevant to the case are discussed with reference to the literature on the subject

I am indebted to Professor Margaret Fairlie for permission to publish this case, to Professor D F Cappell for the report on the specimen, and to both for helpful criticism and advice in the preparation of this paper

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The Response of Isolated Muscle Strips from the Upper and Lower Segments of the Human Full-time Pregnant Uterus to Pitressin and to Pitocin^{*}

BY

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THOUGH the vasopressor and the uterus-stimulating (oxytocic) activities of the posterior lobe of the pituitary have long been known, the chemistry of the active principle or principles responsible for these actions, has remained unsolved. There is even doubt as to whether the posterior lobe contains one or more hormones. Abel¹ and his fellow-workers supported the view that there is only one. Dudley² was of the opinion that there are probably at least three active substances present. Following, however, the publication,³ from the research laboratories of Parke, Davis and Company, that the vasopressor and oxytocic principles had been separated almost completely, the presence of at least two hormones was generally accepted. These two principles, marketed under the trade names "pitressin" and "pitocin," have since been widely used in clinical practice, the former chiefly as an intestinal stimulant and anti-diuretic, the latter as a uterine stimulant especially in cases of pregnancy toxæmia for which the absence of pressor and anti-diuretic properties is clearly an advantage.

OXYTOCIC AND PRESSOR STANDARDS

Pitocin, like the liquid extracts of the

posterior pituitary included in both the British Pharmacopoeia and the United States Pharmacopoeia, is standardized by comparing its oxytocic activity on the excised uterus of a virgin guinea pig, with that of a solution of international standard powdered pituitary, the residual oxytocic activity of pitressin is estimated by the same biological test. The virgin guinea pig is used for this oxytocic assay, a fact that must be emphasized, because in this paper it will be shown that the reaction of the excised human full-time pregnant uterus to pitocin and to pitressin is very different from that of the excised uterus of a virgin guinea pig.

Based on changes observed in the blood-pressure of anaesthetized dogs, a pressor standard⁴ was introduced from the laboratories of Parke, Davis and Company, where it was proposed that 1 mg. of the United States Pharmacopoeia standard powdered pituitary should be considered as containing two pressor units. Though widely accepted in practice, this pressor standard has not been included in either the British or the United States Pharmacopoeias.

During the course of an investigation to study the effect of certain drugs on isolated muscle strips from the human uterus, it was

^{*} Received for publication July 1942

found that pitressin was a powerful stimulant, an observation that has previously been made by other workers on strips from the early pregnant (Robson⁷) and the full-time pregnant human uterus (Adair and Haugen⁸) Moir,⁹ Adair and Davis,⁹ Gardiner and Bradbury¹⁰ and McLellan¹¹ have made similar observations on the non-pregnant, early pregnant, and full-time pregnant human uterus *in situ*

This paper is a preliminary report on a quantitative comparison between the effect of pitressin and that of pitocin on isolated muscle strips from the full-time pregnant human uterus. A striking difference between the reactivity to posterior pituitary extracts of the upper and the lower uterine segments will also be described

MATERIAL

All the muscle strips used for this investigation were removed from the uterus at Caesarean sections performed either by myself or in my presence. Special note was made of the exact part of the uterus from which the strip was taken and the direction of the muscle fibres

The commercial preparations of pituitary used were "pitressin" and "pitocin" (Parke, Davis and Company) obtained from the hospital dispensary. A quantity of more highly purified pitressin (R\ 097376) and pitocin (CE1857), prepared for research purposes and kindly supplied by the manufacturers, was also available, throughout this paper the purified preparations have been used unless otherwise stated. Each c c of "purified" pitocin contained 10 oxytocic units and 0.4 pressor units; each c c of "purified" pitressin contained 10 pressor units and one oxytocic unit.

* One oxytocic unit of posterior pituitary is the same as one international unit which is equivalent to 25 mg of international standard powdered pituitary

METHOD

The tissues obtained were placed in cold Locke's solution and taken to the laboratory. Strips, half to one inch in length, were cut and suspended in oxygenated Locke's solution at a temperature of 37°F, the bath containing 50 c c. Tracings were made by Gimbball levers on smoked drums, contraction of the uterus being recorded by the upstroke of the lever. The time marker recorded intervals of 1 minute. All published tracings are reversed negatives, they should be read from left to right. The temperature in the outside bath was kept constant to ½°F by an electric thermostat. Any tissue not immediately required was kept in the refrigerator (4°C).

Even though the uterine muscle strip was placed in the bath within a few minutes of its removal at operation, several hours usually elapsed before it settled down into its new environment and was contracting steadily. Though the form of the tracing varied with such factors as the length of the strip used, the leverage employed, and the speed of the drum, any response that followed the use of a particular preparation was reasonably constant and did not appear to alter with the varying patterns which the tracing may previously have shown, this is in accord with the findings of other workers. It was regarded as a motor response if the uterus showed either an increase in tone or an increase in the frequency or extent of the individual contractions. An increase in tone was the commonest motor defect observed.

In the Radcliffe Infirmary, the upper segment Caesarean section is rarely performed so the majority of the present experiments were made on muscle strips from the lower uterine segment. This statement requires amplification since all the strips were from patients not yet in labour, and there are some authorities who

do not consider that the lower uterine segment is differentiated until after the onset of labour. For the purposes of this paper, tissue from the lower uterine segment refers to that taken from the uterus well below the attachment of the loose peritoneum covering the front of the organ. Tissue from the upper uterine segment refers to muscle removed well above this level.

REACTION OF THE LOWER UTERINE SEGMENT

When a muscle strip from the lower uterine segment was tested by the addition to the bath (50 c.c.) of $\frac{1}{10}$ th of a unit of pitocin or less, a definite motor response was not observed, with amounts greater than $\frac{1}{2}$ a unit there was a fairly constant slight motor effect. By comparison the result of 2 units of pitressin, added to the bath, was surprising, there was a strong motor response with a prolonged systolic effect, the base line rising to three or four times the height of the original contrac-

tions (Fig. 1). After changing the Locke's solution the experiment was repeated, it was found that $\frac{1}{10}$ th of a unit of pitressin also provoked a powerful motor response, and $\frac{1}{100}$ th of a unit a definite motor effect (Fig. 2). Further trials confirmed this observation. The evidence was clear the pitressin was a more powerful stimulant than the pitocin when tested on muscle strips obtained from the lower segment of a full-time pregnant human uterus.

RESPONSE OF THE UPPER SEGMENT

A study of the reaction of muscle strips from the upper uterine segment showed that, in contrast to the motor effects seen when the lower uterine segment was tested, the addition of comparable amounts of either pitocin or pitressin failed to produce any definite motor response. Large doses of both preparations had a slight motor effect. This difference in reactivity between the upper and lower uterine segments was thought to be of some importance, the

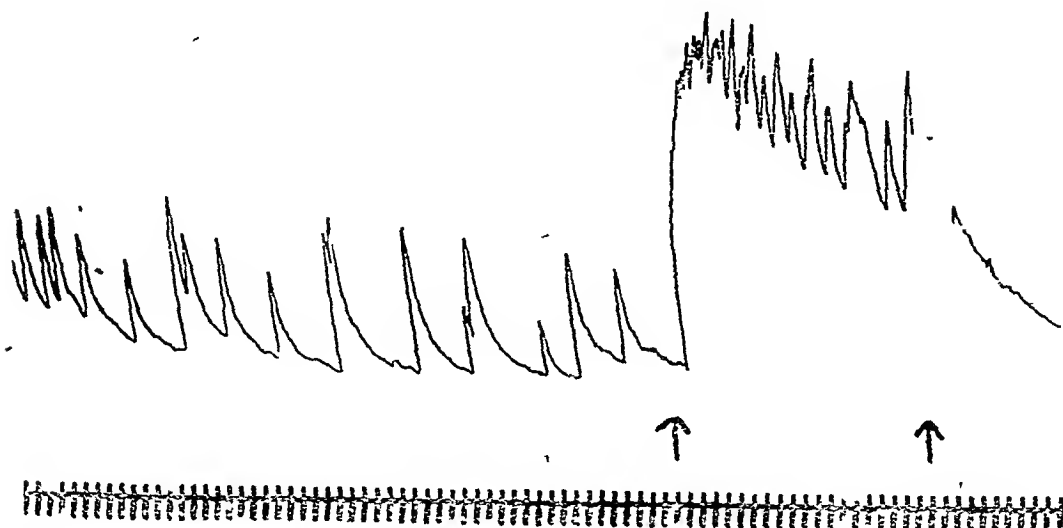


FIG. 1

The response of the lower uterine segment to pitressin (human uterus)

1st arrow

2 units of pitressin

2nd arrow

solution changed

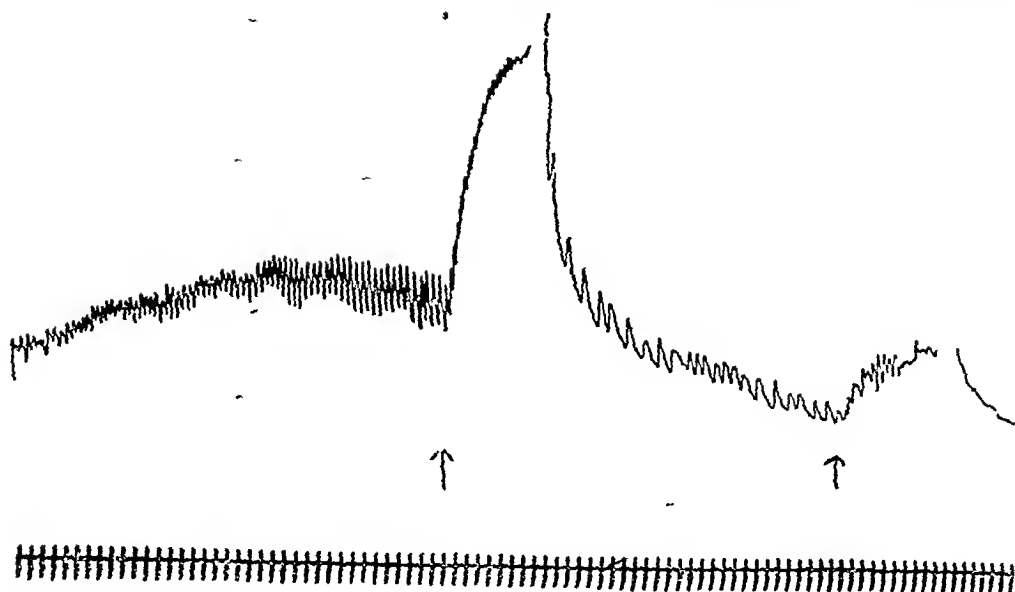


FIG 2

The response of the lower uterine segment to pitressin (human uterus)

1st arrow

$1/20$ th of a unit of pitressin

Solution changed

2nd arrow

$1/100$ th of a unit of pitressin

technique was therefore changed so that clearer proof of this difference might be obtained

COMPARISON BETWEEN THE UPPER AND LOWER SEGMENTS OF THE SAME UTERUS

Instead of a small (50 c c) bath in which the experiments had so far been made, a larger one (100 c c) was used with two hooks on the central rod. Two pieces of uterus could now be suspended in the bath alongside each other, and two independent tracings, the one above the other, obtained under identical conditions. With this technique it was found that active muscle samples from the same part of the uterus reacted similarly to pituitary extracts, thus confirming a previous observation by Adair and Haugen.⁶ No significant difference in reaction was observed between strips cut longitudinally and those cut

transversely. As a search of the literature did not reveal any record of a comparison having been made between the actions and reactions of muscle strips obtained from different parts of the human uterus, and suspended in the one bath, and since the strips from the upper and lower segments had reacted so differently when tested separately, the investigation proceeded along this line.

Two such pieces of muscle from the same patient were now studied, the one strip was from the lower side of a transverse lower segment Caesarean incision, the other was from the upper uterine segment. The first tracings that were obtained from a simultaneous recording of these two muscle strips in the one bath are shown in Figure 3. The upper tracing corresponds to the upper uterine segment, the lower tracing corresponds to the lower uterine segment. The four arrows reading from

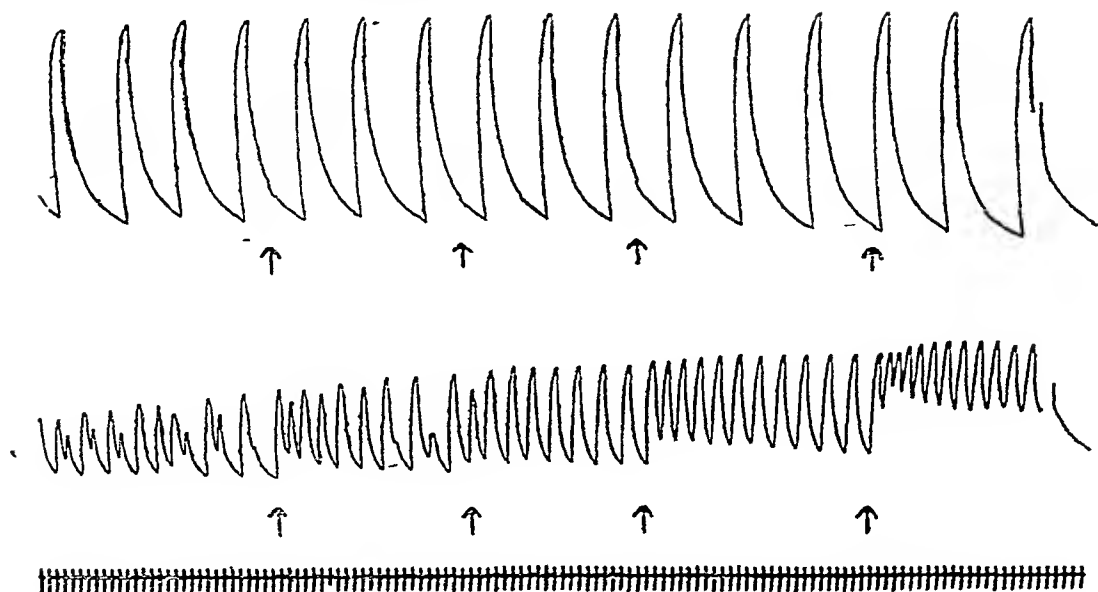


FIG 3

Simultaneous recording of muscle strips from the upper segment (upper tracing) and the lower segment (lower tracing) of the one uterus, showing the motor effect of pitressin on the lower segment and the absence of effect on the upper segment (human uterus)

1st arrow	$1/100$ th of a unit of pitressin
2nd arrow	$1/50$ th of a unit of pitressin
3rd arrow	$1/10$ th of a unit of pitressin
4th arrow	$1/2$ of a unit of pitressin

left to right represent the addition to the bath of $1/100$ th of a unit, $1/50$ th of a unit, $1/10$ th of a unit and $1/2$ of a unit of pitressin. It will be seen that following each addition there is an increase in tone (motor effect) of the lower tracing (lower uterine segment). The upper tracing (upper segment) does not show any response, the pitressin having had apparently no effect. These tracings clearly confirmed the previous findings. After changing the Locke's solution the same two pieces of muscle were tested with increasing amounts of pitocin. Figure 4 shows the results obtained. The 5 arrows reading from left to right represent the addition to the bath of $1/100$ th of a unit, $1/50$ th of a unit, $1/10$ th of a unit, $1/2$ of a unit and 1 unit of pitocin. As in the previous experiment there was no response from the strip

taken from the upper uterine segment.

An important difference between the response of the lower uterine segment to pitocin and the response to pitressin must now be considered in detail. Whereas the strip from the lower segment reacted to pitressin in amounts as small as $1/50$ th of a pressor unit, there was no comparable response to pitocin until $1/2$ of an oxytocic unit had been added to the bath. In other words, in this experiment, unit for unit, pitressin was about 25 times more effective than pitocin in causing the isolated human pregnant uterus to contract. Pitocin, however, contains a residual pressor content equivalent in pressor units to $1/2$ th of the oxytocic activity in oxytocic units, these results could therefore be explained by assuming that most if not all of the oxytocic activity,

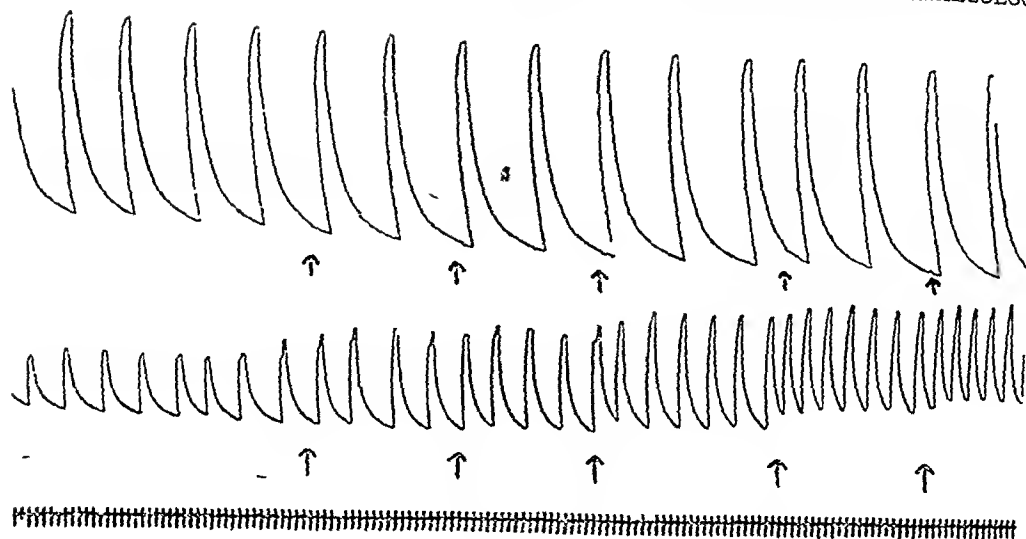


FIG 4

Simultaneous recording of muscle strips from the upper segment (upper tracing) and the lower segment (lower tracing) of the same uterus as in Figure 3, showing the effect of pitocin on the lower segment, and the absence of effect on the upper segment (human uterus)

1st arrow	$\frac{1}{100}$ th of a unit of pitocin
2nd arrow	$\frac{1}{50}$ th of a unit of pitocin
3rd arrow	$\frac{1}{10}$ th of a unit of pitocin
4th arrow	$\frac{1}{2}$ of a unit of pitocin
5th arrow	1 unit of pitocin

for the isolated human uterus, is associated with the pressor principle

Muscle strips from both the upper and lower uterine segments of the same uterus, at or shortly before term, have been available for study on only one other occasion. Figure 5 shows the results obtained, the upper tracing corresponding to the upper segment and the lower tracing to the lower segment. Reading from left to right, the first, second, fourth and fifth arrows mark the addition to the bath of pitressin, whereas the third arrow marks the addition of pitocin. Each time pitressin was added there was a definite motor effect in the lower tracing (lower segment) but the addition of pitocin produced no such effect. The pitressin used for the last addition (fifth arrow) was the ordinary commercial preparation, the response is seen to be

similar to that following the addition of the more highly purified material. As before there was no response from the strip obtained from the upper uterine segment.

The possibility was now considered that pitressin might have acted by inhibiting the action of pitocin. The addition of the latter preparation in increasing amounts was therefore made first, to a strip from the lower uterine segment of another uterus. The result is seen in Figure 6. The first four arrows, reading from left to right, correspond to the addition to the bath of $\frac{1}{100}$ th of a unit, $\frac{1}{50}$ th of a unit, $\frac{1}{10}$ th of a unit and $\frac{1}{2}$ of a unit of pitocin. There was no suggestion of a motor response until $\frac{1}{2}$ of a unit had been added. The fifth arrow corresponds to the addition of 1 of a unit of pitressin. The increase in tone after the pitressin was so pronounced that it

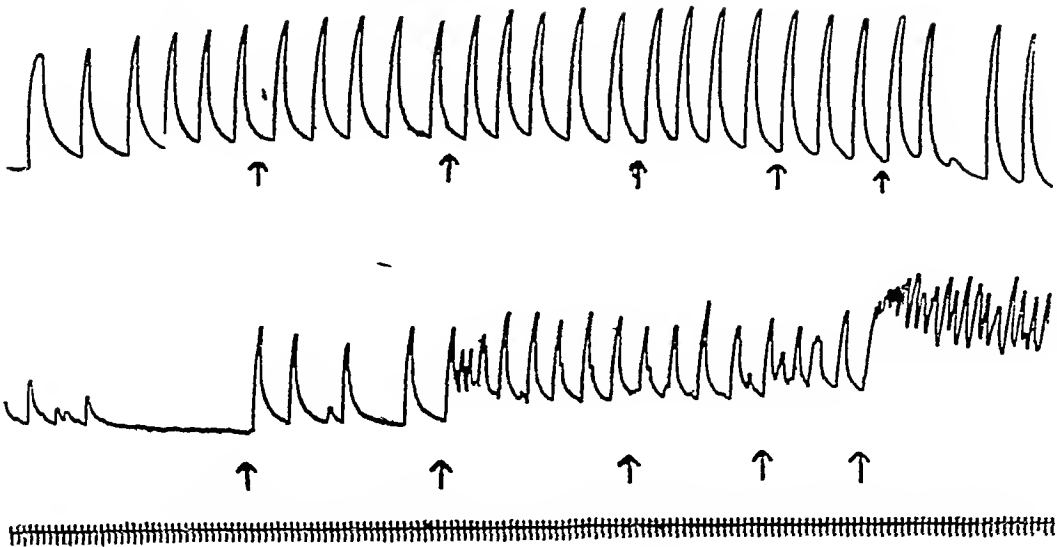


FIG 5

Simultaneous recording of muscle strips from the upper segment (upper tracing) and the lower segment (lower tracing) of the one uterus showing the effect of pitressin and pitocin on the lower segment and the absence of effect on the upper segment (human uterus)

- | | |
|-----------|---------------------------------|
| 1st arrow | 1/100th of a unit of pitressin |
| 2nd arrow | 1/10th of a unit of pitressin |
| 3rd arrow | 1/10th of a unit of pitocin |
| 4th arrow | 1/10th of a unit of pitressin |
| 5th arrow | 5 units of commercial pitressin |

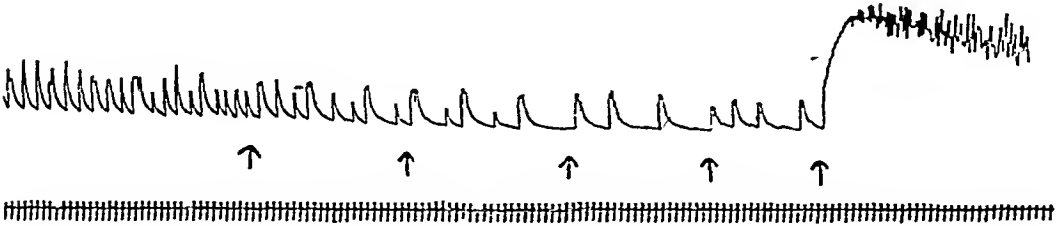


FIG 6

A comparison between the effect of pitocin and pitressin on a muscle strip from the lower uterine segment (human uterus)

- | | |
|-----------|------------------------------|
| 1st arrow | 1/200th of a unit of pitocin |
| 2nd arrow | 1/100th of a unit of pitocin |
| 3rd arrow | 1/10th of a unit of pitocin |
| 4th arrow | 1/2 of a unit of pitocin |
| 5th arrow | 1/2 of a unit of pitressin |

appears reasonable to state that the slight motor effect following the addition of $\frac{1}{2}$ of a unit of pitocin was proportional to, and could be due to its pressor content—equivalent to $\frac{1}{50}$ th of a pressor unit, an amount which on other occasions was known to have provoked a similar minimal motor response

Though it has been possible on only two occasions, at or near term, to obtain muscle tissue from both the upper and lower segments of the same uterus, muscle from one or other part of a uterus has been available for study on many occasions. So far, on over 175 occasions, the action of pituitary extracts—though not always a “purified” preparation—has been tested on isolated strips of muscle from the human uterus, at or shortly before term, the material having been obtained from some 20 cases in which Caesarean section was performed.

When every experiment, in which either pitocin or pitressin was added to the bath, was analysed, it was found that the lower uterine segment, tested 102 times, showed a motor response on 53 occasions (52 per cent), whereas motor effects were observed from the upper segment, tested 70 times on only 9 occasions (13 per cent).

RESULTS OF EXPERIMENTS ON MUSCLE STRIPS TESTED SOON AFTER REMOVAL

These results were of considerable interest and some importance. There were, however, many occasions on which a muscle strip failed to react to any stimulus and it was thought that these failures might be due to differences in the condition of the muscle samples obtained, and particularly to the time between their removal and their use for experimental purposes. A more detailed study showed that, almost without exception, the non-reactive muscle strip had been tested many days after its removal at operation. A further analysis was therefore made of results obtained from pieces of muscle tested within 3 days of removal, and also of the results obtained from strips suspended in the bath within 2 hours of removal. Table I shows the reaction of strips from the upper and lower uterine segments to pitressin and to pitocin

TABLE I
RESPONSE TO PITOCIN

	No response	Doubtful response	Motor response
Upper segment	20	3	3
Lower segment	17	2	17

RESPONSE TO PITRESSIN

	No response	Doubtful response	Motor response
Upper segment	23	4	3
Lower segment	3	4	25

in experiments started not later than 48 hours after the tissue had been removed at operation. It will be seen that the lower uterine segment showed a motor response to pitressin on 25 out of 32 occasions (78 per cent) whereas the response of the upper segment to pitressin was motor on only 3 out of 30 occasions (10 per cent). Even though the figures are comparatively small this difference in reactivity of the two parts of the uterus is significant.

When observations were restricted to muscle strips tested on the day of removal, the results were even more consistent. On 14 occasions, pitressin had been tested on the lower uterine segment and the response was clearly motor in every case, there were no doubtful responses even though as little as $\frac{1}{10}$ th of a unit had been added to the bath. On 13 occasions pitocin, $\frac{1}{10}$ th of a unit or more had been added to the bath, the response was motor on 11 occasions, the degree being more or less proportional to the known pressor content, assuming no activity from the oxytocic fraction *per se*. In 2 cases out of the 13 there was no response to $\frac{1}{10}$ th of a unit of pitocin. On 6 occasions less than $\frac{1}{10}$ th of a unit of pitocin was added to the bath, in no case was there a motor response. On 24 occasions the upper uterine segment was tested with either

pitocin or pitressin and only twice was there a definite motor response—after 3 units of purified pitocin and after $\frac{1}{2}$ of a unit of commercial pitocin, on four occasions there was a doubtful response, and on 18 occasions no response

would produce a motor response the pitocin had *at least* 10 times the uterus stimulating activity of the pitressin (Fig 7) The fractions thus responded normally to the orthodox method of standardization

THE EFFECT OF PITOCIN AND PITRESSIN ON THE VIRGIN GUINEA PIG'S UTERUS

In view of the results described in previous sections, the two preparations used in these experiments were now re-tested, in the same apparatus, by comparing their effect on the isolated uterus of a virgin guinea pig. Using the technique recommended by Burn¹² it was found that the pitocin was *at least* 5 times more powerful as a uterine stimulant than the pitressin, and comparing the minimal amounts that

DISCUSSION

It has been shown that isolated strips of human uterus, obtained during the operation of Caesarean section at or shortly before term, and suspended in a bath of warm oxygenated Locke's solution, exhibit rhythmic contractions which vary in their extent and pattern according to the texture of the individual muscle strip and other factors already mentioned. The response to pitocin and to pitressin of different muscle strips from the same part of the uterus was similar even though the patterns

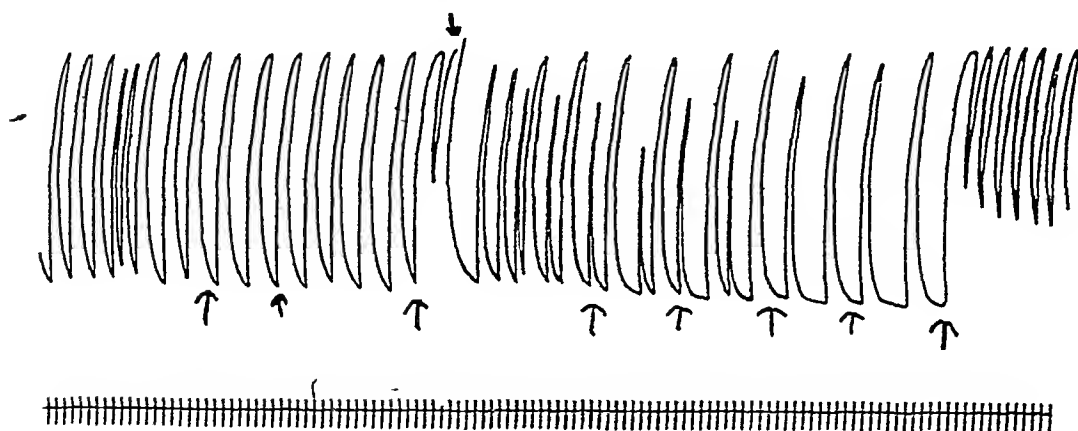


FIG 7

A comparison between the effect of pitocin and pitressin on the isolated virgin guinea-pig uterus

1st arrow	$\frac{1}{100}$ th of a unit of pitocin
2nd arrow	$\frac{1}{50}$ th of a unit of pitocin
3rd arrow	$\frac{1}{20}$ th of a unit of pitocin
Solution changed	
4th arrow	$\frac{1}{50}$ th of a unit of pitressin
5th arrow	$\frac{1}{20}$ th of a unit of pitressin
6th arrow	$\frac{1}{5}$ th of a unit of pitressin
7th arrow	$\frac{1}{2}$ of a unit of pitressin
8th arrow	$\frac{1}{20}$ th of a unit of pitocin

recorded may have varied within wide limits, no demonstrable difference was observed between the response of strips cut from the same uterus, to include a preponderance of circular or a preponderance of longitudinal fibres. When, however, muscle strips from the upper uterine segment and muscle strips from the lower uterine segment were compared by suspending them in the same bath and subjecting them to the same concentration of pituitary extracts, striking differences were observed. Those from the lower segment, immediately after their removal from the body, were found to be sensitive, always reacting to pitressin with a motor response. In contrast, those from the upper uterine segment showed no such response to pitressin.

Robson¹³ found that the reactivity of muscle strips from the lower uterine segment appears to be significantly less than that of strips from the body of the uterus. All his strips from the lower uterine segment, however, had been taken during labour when the lower segment may have been overstretched and damaged, this fact may have accounted for the relative lack of reactivity observed in his experiments.

Adair and Davis⁹ found that the lower uterine segment did not show any response to oxytocic agents, when uterine action was studied by use of a bag introduced into the uterus after lower segment Caesarean section. Their failure to get any response from the lower segment may have been due to this part of the uterus, overstretched after the delivery of the child through it, being temporarily unable to retract down on the intrauterine bag. Possibly they would have been able to demonstrate motor effects if, as the bag was withdrawn from the upper segment, its size could have been increased to fit the stretched lower segment. The operative trauma, the suture line, and the anaesthetic may also

have adversely influenced their results. As their experiments were made on the uterus *in situ* it must be considered whether the response of the isolated muscle strip from the human uterus, as used in this investigation, may be taken to indicate what happens in the intact organ. When the effect of the drug is a direct one, as appears to be the case with pituitary extracts, the reactions in the differing conditions are likely to be the same. Strips from the upper and lower segments were obtained for this investigation under conditions which, though comparable, were not exactly similar, the individual muscle fibres having been stretched more during lower than during upper segment Caesarean section, because of technical differences in the two operations. Either this slight additional irritation to the lower segment, or some hitherto unknown functional dissimilarity between the upper and lower segments, must be responsible for the difference in reactivity of these two parts of the uterus, as the comparison was made under identical conditions.* An overstretched muscle is a damaged muscle which one would not expect to find hypersensitive, therefore it is felt that the evidence suggests that the intact lower uterine segment is in fact more sensitive to pituitary extracts than the upper uterine segment.

Adair and Davis,⁹ who studied the uterine response following lower segment Caesarean section, concluded that so far as human beings were concerned, they could not distinguish between the action of pitocin, pitressin and pituitrin. Indeed they found that pitressin provoked as powerful a response as pitocin and pituitrin even though less had been injected. Some years later, Adair and Haugen⁶ using isolated human uterine muscle strips recorded that the response was usually greater after the addition to the bath of

* See additional note at end

pitressin than after the addition of pitocin, on several occasions they found that a strip of muscle which did not react to pitocin reacted to pitressin. A search of the literature has not revealed any satisfactory explanation of these observations, which have been repeatedly confirmed during the present investigation. It has now been shown that on the isolated full-time pregnant human uterus, pitressin appears to be approximately 25 times more active than pitocin, and that any oxytocic activity the latter preparation may have is not more than would be expected from the pressor substance in it, assuming this to be the principle entirely responsible for stimulating the human uterus.

When the isolated uterus of a virgin guinea pig was tested under similar conditions in the same apparatus the actions were reversed and pitocin was found to be at least 10 times more powerful as a uterine stimulant than pitressin. In other words it may be said that the pituitary fraction, chiefly responsible for the motor effect on the isolated virgin guinea pig's uterus and known as pitocin, has a negligible effect on the isolated full-time pregnant human uterus, compared with that of the fraction that raises the blood-pressure of an anaesthetized dog, known as pitressin. This reversal of effect is clearly of the greatest importance, as extracts of the posterior lobe of the pituitary, perhaps to be used in the induction of labour in women, are at present being standardized for potency against the uterus of the virgin guinea pig.

As the pressor and anti-diuretic properties of the posterior lobe of the pituitary appear to be concentrated in pitressin and as this has now been shown to possess a greater oxytocic activity for the isolated full-time pregnant human uterus than pitocin, it might be claimed with some justification that, in so far as the human

subject is concerned, the evidence suggests that a separation of the pressor and anti-diuretic principles from the oxytocic principle has not been effected. Pitocin however has a greater oxytocic activity than pitressin on the isolated virgin guinea pig uterus. It appears, therefore, that two powerful oxytocic principles, differing in their biological activities, have been obtained from posterior pituitary extracts, the one, concentrated in pitocin, provoking a motor response from the isolated uterus of a virgin guinea pig, but having little effect on the isolated muscle strip from the human pregnant uterus; the other, concentrated in pitressin, provoking a motor response from the isolated human pregnant uterus but having little effect on the isolated virgin guinea pig's uterus. Whether these two principles are similar or dissimilar in composition is a question that cannot as yet be answered.

It is difficult to avoid the conclusion that the further attempt to separate the active principles with a view to obtaining one which contains the oxytocic principles for use in human obstetrics, will be doomed to failure unless controlled by experiments on the human uterus or on the uterus of an animal which shows the same qualitative response to pituitary extracts.

SUMMARY AND CONCLUSIONS

- 1 The reactions to pitressin and to pitocin of muscle strips from the upper and lower segments of the human pregnant uterus, at or shortly before term, have been compared.

- 2 Muscle strips from the human lower uterine segment are much more sensitive to posterior pituitary extracts than strips from the upper segment.

- 3 Pitressin has been found to be approximately 25 times more powerful a stimulant for the human uterus than pitocin but for

the virgin guinea pig's uterus, under the same conditions pitocin was found to be at least 10 times more powerful a stimulant than pitressin. The significance of this has been briefly discussed.

ACKNOWLEDGMENTS

I wish to express my gratitude to Professor J. A. Gunn, Director of the Nuffield Institute for Medical Research, for his constant help and encouragement, without his consent and tuition this investigation would not have been possible. I am also indebted to Professor Chassar Moir, Mr. J. A. Stallworthy, and Mr. G. C. Lennon for valuable criticism and for supplying me with pieces of uterus from cases under their care, to Professor J. Y. Bogue, for his advice and help on technical matters, and to the two laboratory assistants, Maurice Tuckey and Frank O'Connor for their ready assistance.

ADDITIONAL NOTE

Since writing this paper further observations have been made.

1. Further study of the reaction to pitocin and pitressin of isolated strips of the lower segment of the human full-time pregnant uterus has not revealed any difference between those cut before delivery of the child and those cut after the delivery of the child.

2. Two other pituitary preparations (Pitressin R\ 097376, Pitocin R\ 097796) kindly supplied by Messrs Parke, Davis & Co. have been tested on isolated strips of the full-time pregnant human uterus. The Pitressin was found to have a greater activity than pitocin the effect being largely on the lower uterine segment. This was in agreement with the observations already made and described in the present paper.

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Antenatal Thrombophlebitis

BY

J PRESTON MAXWELL, M D (Lond), F R C S (Eng), F R C O G

ANTENATAL thrombophlebitis is a rare disease, and the prognosis in these cases is in doubt, owing to the paucity of material from which to form a definite judgment

Browne¹ speaks thus on the matter "This is a rare complication of pregnancy—the patient is usually a multipara—varicose veins predispose to it. It may, however, start for the first time in pregnancy, and in an apparently normal patient, and affect the iliac, femoral, or saphenous veins, usually of one side. Neither is there any special predisposition to the development of phlegmasia in the puerperium."

The following case is presented as an addition to our knowledge of the condition

Mrs K B a 4-gravida was admitted to the White Lodge Hospital (E M S) on May 5th 1942 suffering from antepartum thrombosis of the superficial saphenous system in both thighs. This thrombosis extended up to the saphenous opening on both sides and down as far as the knee. Not only was the great saphenous vein palpable, as a hard tendon cord, but the lateral branches were also affected. There was practically no oedema of the lower legs and feet but she had already been in bed for one week. The condition started with redness and pain on the inner surface of both thighs. A cause was not found. The patient was in good health the blood-pressure normal and there were no prominent varicose veins in either leg. A catheter specimen of urine showed a faint cloud of albumin there were no casts but a few leucocytes. Culture showed a very scanty growth of bacillus coli and staphylococcus albus. Her blood sedimentation rate was 1st hour 27 mm 2nd hour 60 mm her blood count was normal and she was not anaemic. A septic focus was not found though a careful search was made.

The pregnancy was a twin one. She was kept at rest in bed, and by the middle of June the thrombosis had disappeared, and there was nothing to note about the legs,

save a slight oedema of the lower leg. A trace of albumin persisted, and the blood-pressure was normal. She was then allowed up and about, and was walking steadily and well.

On July 13th, 1942, a fortnight before her expected date, she went into labour and was delivered of twin girls, the first presenting by the head, and weighing 5 $\frac{3}{4}$ pounds, the second presenting by the breech, and weighing 5 $\frac{1}{2}$ pounds. Both children progressed well. The placenta was a single one, a single chorion and two amnions. There was no excessive haemorrhage. The patient made a rapid and satisfactory recovery without incident, and she left the hospital well on the 18th day of the puerperium, there was no sign of trouble in the legs.

She was able to nurse both children, and was so doing 6 weeks later when she was in good health. The children were progressing normally. Her previous pregnancies had been —

- (1) A twin one (girls), carried 5 months only
- (2) A 9 pound girl, alive and well, now aged 7
- (3) A 9 pound girl, alive and well, now aged 5

The interesting points of the case are the very marked thrombophlebitis, and the fact that there was no sign of recurrence after labour. The only treatment given was a capsule of adexolin twice a day, and a tablet of ascorbic acid thrice daily.

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D R C O G Examination, March 1943

Harrison Broadbent	Jean Ann Forbes	A S Minabbawy
Walter Calvert	Agnes J M Gilruth	Joyce G Neil
Nora H C Clarke	Irene D M Hastilow	Erica M Roberts
Frank Blair Davidson	Mary M Lynch	Edith Taylor
Gerald S W Evans	Irene E Howorth	Marv U Wilkin

The following were formally admitted to the Fellowship by the President

Gladys Hill	Norman Lewis White
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Janet Elizabeth Bottomley	Louis Resnick
Phyllis Dingle	Gordon Short Sturtridge
Marjorie Olive Dunster	Kenneth Gordon Patrick Worner

Arthur James McNair	John Chassar Moir
Arthur Alexander Gemmell	Robert Henry Joseph Mulhall Corbett

Bryan Leslie Jeaffreson James Sinclair Quinn

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BOOK REVIEWS

A Textbook of Gynaecological Surgery By
SIR COMINS BERKELEY and VICTOR BONNEY
Fourth edition 574 original drawings by Victor
Bonney and 17 coloured plates 1943 Cassell
& Co Ltd London, Toronto, Melbourne and
Sydney

THE idle turning of the pages of the new edition of this famous gynaecological operative surgery and a glance at the illustrations which so lavishly adorn the book are sufficient to evoke sentiments akin to those aroused in Keats prompting the famous lines in *On Reading Chapman's Homer*. The surgeon who reviews this work still recalls the thrill of pleasure and admiration produced by the appearance of the first edition and tenders his tribute to the authors for the immense aid which the book has rendered not only to gynaecological surgeons but also to those whose surgical labours range over a wider territory of the body than the female pelvis.

A feature of the present edition is the conservative attitude adopted in the treatment of many of the problems of pelvic pathology. A growing appreciation of the manifold functions of the ovary has led gynaecological operators not too soon to exhibit a greater reluctance to remove these structures, and the reproach is at length removed from those who practise this important branch of surgery that a snowflake in hell has a better chance of survival than an ovary in a gynaecological operating theatre.

This conservatism has also extended to the uterus in the treatment of many myomata and also to the diseased or damaged Fallopian tube. One of the two authors performed myomectomy for fibroids 379 times with a lower mortality than the microscopic death-rate attending sub-total hysterectomy and of those patients within the child-bearing age desiring children after this operation no less than 38 per cent conceived and 75 per cent of the children were born normally.

The anæsthes attendant upon the Baldwin-Morrison operation for absence of the vagina have been

removed by McIndoe's plastic operation, and although the authors describe in detail the former operation they make it clear that it has been relegated to the limbo of the past by this new contribution from the plastic surgeon's art.

It is not within the province of the reviewer to enter into the debate between radiotherapy and the Wertheim operation for carcinoma of the cervix. Carcinoma of the cervix is a very common malady the radium technique is very easy and yields results better than an imperfect radical operation, and there are few surgeons in the world who have had the experience of the Wertheim operation which the distinguished authors of this work enjoy. The operation is perhaps the most exacting of all gynaecological procedures and to the surgical onlooker it would appear that the Wertheim operation which yielded such good results in the hands of Berkeley and Bonney at a mortality rate of 14 per cent in a long series is now likely to pass into desuetude.

No detail is omitted of the operative and non-operative methods required to deal with difficulties encountered during laparotomy or embarrassing the convalescence. One of the authors was among the pioneers of enterostomy for post-operative ileus the technique of reimplantation of the sectioned ureter into the bladder is described and well-illustrated. The Paul-Mikulicz exteriorization type of large bowel resection is somewhat fashionable with abdominal surgeons just now but the authors prefer end-to-end suture.

The patients of the two authors were never wont to grow much older during the progress of their operations these surgeons learned from their master Sir John Bland-Sutton the importance of time and their own mantle has descended upon many disciples. The speed of the modern gynaecologist contrasts with a slow school of surgery which has grown up and makes him a most valuable asset in the abdominal surgery of total war many excellent cases already stand to their credit in this sphere of traumatic surgery.

Reference has already been made to the excellent illustrations for which one of the writers is responsible these must have been a guide and beacon to many a less experienced operator and must have kept many a surgical fee out of the pockets of the authors

G GORDON TAYLOR

'Midwifery for Nurses' Third edition By
DOUGLAS MILLER M D F R C S (Edin),
F R C O G Edward Arnold and Co 7s 6d

THIS book is a useful introduction to the theory and practice of midwifery. The fact that throughout the book the writer refers to the nurse and never to the midwife leads one to presume that it is intended for the maternity nurse and not the practising midwife since the information it contains is insufficient to meet all the requirements of the pupil studying for the Central Midwives Board first and second examinations, or to serve as a reference book for the qualified midwife.

Some of the statements regarding treatment are

misleading. Removal of retained membrane from the uterus immediately following the 3rd stage of labour is contrary to the teaching in most training schools. Sylvester's method of artificial respiration is generally considered quite unsuitable for the asphyxiated baby, and the use of a warm bath in asphyxia pallida. Experience does not support the assertion that immersion of the baby at the daily bath is liable to cause infection of the cord.

In the section on abortion the period of viability is given as the 30th week of pregnancy whereas the legal definition of abortion is the termination of pregnancy before the 28th week, and this is accepted by Insurance Companies in respect of the payment of the maternity benefit.

The section on the physiology of labour is particularly clear with the diagram describing the dilatation of the cervix, so also is the chapter on the clinical course of normal labour. It is disappointing that in the management of normal labour reference is not made to the use and action of sedative drugs which a midwife, acting as such, may administer.

E A C-K, S R N S C M

REPORTS ON HOSPITALS AND DEPARTMENTS OF PUBLIC HEALTH

THE REPORT OF THE ROTUNDA HOSPITAL FROM 1ST NOVEMBER, 1940 TO 31ST OCTOBER, 1941

THIS report which appears with unfailing regularity hardly needs introduction. The high standard set by his predecessors has undoubtedly stimulated the new Master Dr Falkner and we congratulate him on his achievement. The report records with regret the death of Sir William Smyly who had maintained a life-long interest in the Rotunda and whose Mastership coincided with the changes that ensued as a result of the introduction of asepsis and antiseptics into obstetrics. A richly deserved tribute is paid to Dr Davidson the retiring Master. Structural additions to the hospital include a new lecture room and a new pathological laboratory, the old having been refitted as a research department. A new department for premature and sick babies has been completed. An example all maternity units would do well to copy in an effort to lower the grievously high mortality that still prevails among the premature. The report although principally concerned with the maternity work includes an account of the work of the gynaecological paediatric, pathological and X-ray departments.

The total number of attendances in the Out-patient Department shows a decrease to which no particular significance may be attached. An investigation of the Wassermann reaction in 800 consecutive cases is mentioned. Surely the time has come for all antenatal patients to have their blood reaction tested? The significant fact that 50 cases of syphilis were treated suggests the urgent need for the adoption of this test as a routine investigation.

Mention is made of the excellent work done by the Social Service Department surely justifying extension of these services which are only restricted in most hospitals by financial considerations. The In-patient Department admitted 3,896 patients of

whom 3,536 were delivered, 12 mothers died. The district deliveries numbered 1,530 none of which ended fatally, a tribute to the excellence of the domiciliary practice.

There follows a most interesting account of the various presentations and obstetric abnormalities and mention is made of the treatment carried out. One is sorely tempted to make adverse comments when the procedure adopted is not in keeping with one's own methods while a similar urge to applaud is felt when agreement with one's view is apparent. This is exemplified by one's horror at the use of Bougie induction, particularly in cases of disproportion and more so when lower segment section was required on one occasion to deliver the patient. Unanimity over the restricted use of quinine for medical induction restores good feeling. Similar examples could be repeated over and over again but any obstetrician anxious to improve his art is urged to read the report in its entirety and then to search himself. Would he list albuminuria as an indication for delivery by the forceps? Primary inertia is not defined in terms of hours in the 1st stage of labour but merely as prolonged labour. The conservative attitude described is to be commended, but no mention is made of any specific remedies such as the oestrogens. Mention is not made of the dietetic treatment of pre-eclampsia still referred to as albuminuria. Has the high protein salt-free diet not found a place in the Dublin treatment? Energetic and early treatment with the sulphanilamides appears to have been successful in the treatment of puerperal sepsis. No deaths occurred in spite of several instances of haemolytic streptococcal infection. The maternal mortality for booked cases was 0.11 per cent which contrasts markedly with 1.13 per cent for emergency cases. In the gynaecological department there were 617 admissions and of these 553 were operated upon. We note that Wertheim's hysterectomy still has a place in the surgical activities of the Rotunda. The

appointment of a blood-transfusion officer has many advantages, but it limits the opportunities for junior residents to give transfusions experience which might prove invaluable in their future practice Dr Falkiner concludes his summary of his year's work with a well-deserved tribute both medical and nursing, the excellent standard of past years having obviously been maintained

Dr W R F Collis has contributed a short account of the paediatric department Mention has already been made of the opening of the new nurseries exclusively for the treatment of abnormal babies This is an important advance, and we hope that the more complete records to be available soon will demonstrate the value of this step The pathological department's statistics indicate the increasing value of laboratory investigations in obstetrics and gynaecology Comment has already been made on the need for instituting a routine Wassermann reaction The report concludes with a list of the number and variety of radiological examinations performed further evidence of the value of such a department in all modern maternity departments

REGISTRAR'S REPORT, LIVERPOOL MATERNITY HOSPITAL YEAR ENDING DECEMBER 31ST, 1941

THIS report reflects the effect of enemy action on the work of a large maternity hospital, namely a decrease in the total number of patients, but a greatly increased number of emergency admissions The statistical summary states that 2,624 patients were attended by the hospital, 955 in their own

homes (the latter figure corresponds with the figure given in the district report), and 1,669 in hospital The latter figure is then analysed into 1,502 patients booked, and 617 emergencies which is clearly inaccurate It would seem that the figure should be 1,025 and not 1,502 The tabulated records of the various abnormalities provided some points of interest In the section on heart disease Caesarean section was the treatment in 25 per cent the actual number of cases being small but the percentage is relatively high Colonic lavage once advocated in Dublin, and more recently almost renounced by them is employed in the treatment of eclampsia nevertheless the patients recovered A set technique is described for breech delivery, and maintenance of traction after the birth of the buttocks is included surely traction is to be avoided particularly at this stage A breech mortality of 7.4 per cent is impressive until the total figure of 25 per cent is arrived at by means of a little mental arithmetic In the copy of the reports received, page 11 must be looked for between pages 44 and 45 A maternal mortality of 0.4 per cent for booked cases is relatively high, but it is unusual to encounter 2 cases of liver atrophy in 1,500 cases Details are given of all the fatal cases one attributed to obstetric shock is very puzzling and makes one wonder whether it is advisable to give such a quantity of blood (3 pints) to a patient in whom there was no bleeding The report concludes with a paediatric section It would be interesting to know if the Rhesus Factor was investigated in the 3 cases of icterus gravis Perhaps it is not too late now to determine the parental reactions We are not familiar with the heading 'genital crisis' which seems to include mastitis, hydrocele and malana within its scope

Review of Current Literature

Director FREDERICK ROQUES M A , M D , M Chir (Cantab) , F R C S , F R C O G

THIS Review contains the lists of contents and abstracts of the more important articles from the journals with which the *Journal of Obstetrics and Gynaecology of the British Empire* exchanges

The Review of Current Literature has kept the readers of the Journal in touch with current literature throughout the world owing to the war many

journals with which the *Journal of Obstetrics and Gynaecology* previously exchanged are no longer received At the end of the year an Index of all the subjects contained in the articles of the journals reviewed is printed Arrangements are also made to include abstracts of important articles, on borderline subjects, such as Physiology, Biology and Biochemistry

LIST OF ABSTRACTORS

J LYLE CAMERON, F R C S,
W E CROWTHER M B
R H B ADAMSON, M D
B JEAFFRESON, F R C S

P MALPAS, F R C S
T N A JEFFCOATE, F R C S
MEAVE KENNY F R C S
JANE H FILSHILL

The Canadian Medical Association Journal

Vol xlv March 1942 No 3

An improved radical technique for carcinoma of the external genitalia in the female H W Johnston

AN IMPROVED RADICAL TECHNIQUE FOR CARCINOMA OF THE EXTERNAL GENITALIA IN THE FEMALE

Carcinoma of the external genitalia is a rare disease and is confined almost entirely to elderly women The growth begins as a nodule a wart or an ulcer, and in more than 50 per cent of cases it follows leukoplakic vulvitis

Treatment demands removal of the primary growth and the lymphatic glands which drain the vulva The lymphatic drainage is very rich anastomosing freely and a growth on one side may invade the glands in both inguinal regions

There are two groups of inguinal glands superficial and deep The superficial glands are from 10 to 20 in number, lying immediately below Poupart's ligament Several of these lying over the fossa ovalis are usually very large The chief drainage into these glands is from the vulva The deep glands usually known as the glands of

Cloquet lie medial to the femoral vein They receive lymph from the superficial glands and directly from the regions of the clitoris and the urethra Their removal is usually difficult and was formerly considered in many cases to be impossible Bassett introduced the technique of dividing Poupart's ligament to expose these glands and facilitate their removal There is however some difficulty in restoring Ponpart's ligament afterwards

In thin patients palpation and removal of these glands is simple In fat patients it is essential to remove a large T shaped mass of fat which enmeshes the glands The horizontal part of the T lies below Poupart's ligament, the vertical part over the saphenous opening

The majority of patients with cancer of the vulva are poor operation risks and a procedure is here described which permits speed and extensive removal of the primary growth with its draining lymphatics

An incision is made an inch below Poupart's ligament extending from a point below the pubic spine to a point below the anterior superior iliac spine The skin on each side of the wound is

dissected free from underlying fat and well retracted. This exposes in the groin a mass of fat adherent to the abdominal fascia above, Poupart's ligament centrally, where the adherence is very dense, and to the fascia lata below. This mass of fat is dissected with the aid of scissors from the underlying structures. Usually the dissection is started at the upper part carried downwards and then medially. As the fat is raised from its bed and drawn medially, the long saphenous vein will be clamped and divided together with another small vessel penetrating the fascia lata. This mass of fat is drawn medially, exposing the saphenous opening which is cleared of fat and glands by gauze dissection. All the fat as far as the symphysis pubis must be removed at the same time together with the areolar and fatty tissue of the outer part of the vulva, where there are many small glands. The mass of fat will have the appearance of the letter T, the horizontal part being the tissue which occupied the region above and below Poupart's ligament while the vertical limb of the T will be the tissue lying along the saphenous vein. Three superficial vessels will require division and ligation: the superficial epigastric, the superficial circumflex iliac and the external pudic. The long saphenous vein will also be divided and ligated as this permits a freer exposure.

The femoral vein is drawn gently outward with the left index finger and Gimbernat's ligament is divided with a pair of curved scissors, thus exposing the deep inguinal glands. Occasionally an abnormal obturator artery will be present it runs downwards along the front of Gimbernat's ligament at about its centre. The possibility of its presence must be kept in mind.

The deep inguinal glands lying medial to the femoral vein are removed with the finger assisted by traction with a pair of ring forceps. The inguinal ring is also explored as on rare occasions a gland is found in this region. Through the ring also the peritoneum may be lifted upwards and further removal of areolar tissue effected.

The boundaries of the femoral ring are defined the divided Gimbernat's ligament repaired by suturing the part of Poupart's ligament medial to the femoral vein to the medial portion of the ileopectineal fascia. Its closure is completed with three or four interrupted stitches. All these

manipulations should be conducted with great care to avoid not only penetrating the femoral vein, but exerting undue prolonged pressure upon it as this might cause stasis and thrombosis. The inguinal ring is closed with interrupted stitches and the edges of the deep fascia are approximated. The skin wound is closed with one continuous and four or five interrupted sutures of black silk. A small drainage tube is left in the inner end of the wound, as exudation of serum is always copious. The same procedure is carried out on the opposite side.

The patient is placed in the lithotomy position and the vulva is excised. Two oval incisions are made, one around the entrance of the vagina and passing in front of the meatus urethrae after leaving a fairly wide margin of mucosa, the other and outer incision passes wide of the growth around the whole vulva. A bridge of skin may be left across the perineum except in cases of leucoplakia. The greater and lesser labia are dissected free and removed. The dorsal vessels of the clitoris are of considerable size and must be carefully ligated. Freely oozing areas are under run with catgut and tied.

The wound in the vulva is closed with interrupted stitches of silkworm gut and a few catgut. In front of the urethra the skin edges on each side are approximated, while behind the urethra the cut skin is sewn to the divided edge of the vagina. It there is difficulty in bringing these edges into coaptation, under-running the skin, or in the worst cases, lateral incising of the skin will suffice to effect adequate relaxation. The sutures round the urethral orifice require careful placing.

When the urethral orifice is involved a modification of the anterior part of its inner incision will be required. The anterior part of this incision does not pass in front of the urethra, but through the vaginal wall behind it and the urethra is transected at about its centre, permitting removal of the greater portion of this tube. Much free oozing will result and is controlled by passing surrounding sutures of catgut. A new meatus is fashioned by suturing the mucosa of the urethra to the anterior part of the vaginal mucosa which has been cut with convexity forwards, so as to permit readily of reconstruction. Undercutting of the vaginal mucosa may occasionally be neces-

sary to avoid tension Black silk is the best material for sutures

Eighteen very excellent serial drawings to illustrate the steps of the operation are included

Vol xlv June 1942 No 6

*The treatment of acute and chronic salpingitis
A B Nash

TREATMENT OF ACUTE AND CHRONIC SALPINGITIS

The commonest cause of pelvic inflammation is the gonococcus This organism has a predilection for mucous surfaces and for the sub epithelial tissues of glands Here these organisms retain their infective potentialities for a long time, even after all external signs have ceased to be in evidence Secondary pyogenic infection is liable to occur It is this persistence of the gonococcus which causes recurring attacks of salpingitis, so that the acute stage may pass into the chronic phase which is so liable to be attended by occlusion of the Fallopian tubes, damage to other structures and loss of function It is important therefore, to treat adequately the primary infection in the cervix

When there is acute infection of the genital tract, the patient should be kept in bed and examination and the use of instruments must be strictly limited as the passage of specula and the application of medicaments to any part of the genital tract will not only fail to eradicate the disease in the lower tract but will increase the chances of its spread to the Fallopian tubes Even the use of sulphonamides has not yet been shown to eradicate the disease so quickly and completely that these precautions mentioned may be neglected with safety It is no less important to enjoin strictly total continence absence from alcohol excitement exposure to cold physical exertion and fatigue This applies particularly to a time near the menstrual period These are factors contributing greatly to the occurrence of salpingitis The case however must not be regarded as hopeless with regard to preservation of child bearing function There is a tendency for acute salpingitis to subside spontaneously provided that no fresh infections are superimposed and that the lines of treatment which have been given be followed The beneficial effects of the

sulphanilamides does not permit of laxity in employing these other methods of treatment Both methods should be complementary, and rest in bed should be maintained for several days after the subsidence of fever pain leucocytis, and increase in sedimentation rate, and it should be employed before during and after menstruation for the next two or three periods, at which times exacerbations are liable to occur Fowler's position should be employed, ice bags applied to the lower abdomen, and pain and rectal tenesmus relieved by aspirin codeine, or even tincture of opium

Surgery has no place in the treatment of acute gonorrhoeal salpingitis, nor has the author any good opinion of the employment of heat as a therapeutic measure

When the Fallopian tubes become sealed, there is little hope of retaining or retrieving fertility Pylosalpinx, hydrosalpinx tubo ovarian abscess extensive adhesions of the pelvic peritoneum and viscera are liable to occur The ovaries may become involved in the inflammatory process By this time the function of fertility must be regarded as destroyed All this entails much suffering for the patient and finally relief may be obtained by the employment of only the most radical type of surgery

Whatever type of treatment is employed it is liable to be minimized by physical exertion alcohol, fatigue and sexual stimulation The author is of the opinion that sulphanilamides in the chronic type of inflammation are of limited benefit, but heat by one of several methods is of some use Non-specific protein therapy is of small value It seems that time patience the avoidance of reinfection and aggravating influences are the most important elements in the treatment of chronic inflammation None are easy to employ or to enforce, nor are they spectacular in their effects and seldom are they utilized to their full extent

Surgery should not be invoked until the methods cited have been given a full and competent trial and especially until all inflammatory processes have subsided But when resort is made to operative measures these must be adequate Half measures only entail the necessity of further operation As the ovaries are usually seriously damaged their conservation is liable to be followed by major menstrual aberrations When no part

of an ovary can be conserved, the uterus is of little value and the cervix, it must be remembered, is chronically infected. Total hysterectomy, therefore, has to be considered.

Pyogenic salpingitis, acute or chronic, presents many of the problems already outlined.

Tuberculous salpingitis is not so uncommon as is usually believed. It is thought to occur as frequently as once in every 20 cases of salpingitis although opinion on this point varies widely. When there is pronounced pulmonary tuberculosis the lung affection must receive first consideration. Sanatorium treatment must have its place. X-ray therapy in this condition is again a subject of extensive controversy. The difficulty of accurate diagnosis of tuberculous pelvic disease has a considerable bearing on radio therapy. Most authorities agree that surgical treatment is indicated in

the majority of cases. Pulmonary tuberculosis or extensive peritoneal involvement are contra indications. Vaginal coeliotomy should not be performed as fistula formation is liable to result. Radical or limited surgery is again a matter of controversy but apparently the majority of experienced surgeons favour extensive eradication. Ovaries at all affected are better removed. Dense and unyielding adhesions are almost certain to make any operation extremely difficult. Drainage of the peritoneum is condemned by the majority of surgeons. There are great difficulties in determining the extent of the disease even when the organs are exposed to view and touch. Reproductive function is usually irrevocably lost long before the case is even diagnosed.

An eighteen-item bibliography is appended.

J. LALE CANEFOX

Medical Journal of Australia

September 7th, 1940

*Haemorrhagic disease of the newborn

October 19th, 1940

Effects of testosterone propionate on pouch scrotum clitoris and penis of trichosurus vulpecula. A. Bolloger and A. Carrodus.

*Hydranencephaly. H. F. Bettinger.

The significance of the Aschheim-Zondek test in the early diagnosis of chorionepithelioma. W. G. Cuscaden and H. F. Bettinger.

May 2nd, 1942

*Congenital lacunar skull. H. B. Bettinger.

May 23rd 1942

*Granulosa-cell carcinoma of the ovary, with the report of a case. R. Mackay.

June 13th 1942

Mesonephroma of the ovary. Current comment.

prothrombin in the plasma depends upon the presence of vitamin K in the diet and its absorption by the bowel. It is absorbed from the bowel only in the presence of bile salts.

The cause of physiological hypoprothrombin aemia of the newborn is obscure. It would appear that the placenta forms a barrier to the free passage of prothrombin from the maternal circulation to that of the foetus. High vitamin K feeding of the pregnant mother does appear to increase the amount of prothrombin in the blood of the newborn.

In an established case of haemorrhagic disease of the newborn the administration of vitamin K by mouth appears to be of value in the less severe case while more rapid increase of foetal prothrombin is secured by transfusion with normal adult blood.

HYDRANENCEPHALY

Bettinger describes the case of a first born child of a healthy mother of 21 years.

Labour was easy and spontaneous, and the foetus was, at birth, considered to be normal in all respects except that the cranial sutures were if anything a little wide apart. It took the breast like any normal child but its head was noticed to

HAEMORRHAGIC DISEASE OF THE NEWBORN

Under the heading of "Current Comment" a short review of the clinical manifestation of this condition is given. It is pointed out that in all such cases there is an excessive deficiency of prothrombin in the infant's blood, and this is thought to be the cause of the bleeding.

The ability of the liver to maintain the level of

feel cooler to touch than the head of other newborn babies. For five days it developed quite normally, then for two days it had a subnormal temperature and death occurred on the seventh day without any definite symptoms or signs.

On postmortem examination when the skull was opened, the dura mater was very firmly attached to the inner surface of the bones and no trace of the cerebral hemispheres could be found. At this point it was decided to postpone further examination of the contents of the cranial cavity until the whole head had been hardened. After hardening the head was bisected. It was then seen that the cerebral hemispheres and the corpus callosum were completely absent, some mid-brain tissue was present below an obscuring membrane, but normal structures could not be recognized here. The pons, cerebellum and medulla oblongata were apparently normal. The thorax and abdomen contained no abnormality.

Histological examination of the cranial structures was not made as this could only have been carried out at the expense of destruction of the whole specimen.

The writer considers that in view of the presence of well-formed membranes and skull the condition must have arisen late in pregnancy and he suggests that it may represent a very advanced degree of porencephaly.

The description of this case is illustrated by three very good photographs of the external view of the head and both halves of the sections of the head after hardening, with the structures *in situ*.

CONGENITAL LACUNAR SKULL

Bettinger describes the case of a primipara aged 20 years delivered of a female child at the eighth month of pregnancy. The child had a spina bifida in the lumbar region and marked bilateral talipes. The child survived 7 days and during this time it developed a steadily increasing tension of the fontanelle and signs of inflammation of the spina bifida.

On post mortem examination except for the presence of a horse shoe kidney abnormalities were confined to the skeleton. The feet were in extreme talipes and in addition to the spina bifida in the lumbar region there was a sharp angled kyphosis in the same region. The skull was the site of the most striking abnormality. After removal of

the scalp a large number of slightly bulging areas was seen. These were covered only with a thin membrane and no bone. A number of these areas were oblong shaped and arranged symmetrically on both sides of the mid line in the parietal bones and more irregularly in the frontal and occipital bones. On removal of the vault of the skull the areas appeared as deep cavities lined by thick smooth ridges of bone. The convolutions of the brain were flattened to correspond to these depressions. After removal of the brain a gross exaggeration of the configuration of the base of the skull was seen. All the grooves were deeper and all the ridges more prominent than usual but the condition was less marked than in the vault. A horizontal section through the brain showed a considerable degree of hydrocephalus.

After giving a short resume of all the theories that have been advanced to account for the occurrence of lacunar skull the writer concludes that the following explanation is correct.

Towards the end of pregnancy there is non-physiological incongruity between skull and brain. Under normal conditions localized incongruities do not occur because the cerebrospinal fluid acting as a water cushion ensures an equal pressure upon all parts of the cranium. In the case of a meningocele the escape of cerebrospinal fluid into the sac allows the brain to come into direct contact with the inner surface of the vault. Additional space for the growing brain cannot be obtained by bulging of the non-osseous parts of the cranium because the surrounding amniotic fluid does away with all pressure differences. Erosion of the bone by pressure atrophy will therefore occur wherever the gyri press most closely against the inner table. A typical lacunar skull will then develop.

GRANULOSA-CELL CARCINOMA OF THE OVARY WITH THE REPORT OF A CASE

Mackey reports the case of a single woman of 32 years complaining of bleeding *per vaginam* for 6 months. The periods started at 13 years and had always been irregular and accompanied by dysmenorrhoea. Three years before at the age of 29 years she started a period of amenorrhoea which lasted two years followed by irregularity for one year.

On examination blood was found to be coming from the cervix, the uterus was slightly enlarged

and a freely movable tumour the size of a foetal head could be defined in the posterior form. In view of the patient's oestrogenic disturbance a diagnosis of granulosa cell tumour of the ovary

was made and this diagnosis was confirmed at operation

The macroscopic and microscopic features were typical
R H B ADAMSON

American Journal of Obstetrics and Gynecology

Vol 41 No 3

*The effects of analgesia on the newborn infant
C O McCormick

A report on a series of complete tears of the perineum with extension up the posterior vaginal wall repaired by the vaginal flap method
R E Campbell

Acidosis and alkalosis in obstetrics and gynaecology W T Pride, J R Reinberger and D T Holland

Home delivery service for medical students
C R Hannah

Nationality and carcinoma of the cervix F R Smith

*A skin test for the diagnosis of pregnancy F H Falls, V C Freda and H H Cohen

Objections to induction of labour in normal pregnant women E L Cornell

Pubertas precox due to ovarian tumours C B Lull

Actinomycosis of the ovary W A Coventry

The treatment of pelvic endometriosis W T Dannreuther

The effect of combined administration of chorionic gonadotropin and the pituitary synergist on the human ovary C Mazer and E Ravetz

A comparative study of male and female pelvis in children with a consideration of the aetiology of pelvic conformation D G Morton and C T Hayden

Some observations on the gynaecic employment of equine gonadotropins E C Hamblen

Menstruation and urination through a clitoris-like structure D N Barrows and W N Bloch

Amenorrhoea and sterility caused by bilateral polycystic ovaries M L Leventhal

Meigs syndrome F R Lock and C G Collins

Fulminating systemic haemolysis following incompatible blood transfusion M Fellman

Dermoid cyst of the ovary with squamous cell carcinoma S Brody

Herpes gestationis S J Turner and S J Zakon

Diabetes insipidus complicating pregnancy S D Hart and H B Breitman

A study of puerperal mortality in New York City (1937-1940) with especial reference to preventive factors R G Douglas

Puerperal mortality in the Borough of Brooklyn City of New York C A Gordon

Society transactions

Selected abstracts Ectopic pregnancy

THE EFFECTS OF ANALGESIA ON THE NEWBORN INFANT

McCormick says that no single issue divides obstetricians so much as that relating to the use of analgesia some do not use it and criticise it severely while others use it and praise it loudly. One of the main arguments against its use is its supposed bad effect on the child. Those who use it maintain that this supposition is erroneous, although there is no doubt that it does cause some delay in the initial respiration and yet no proof for or against this statement has been forthcoming. In this paper the author does bring forth evidence, not only that it is harmless to the child but also that it is actually beneficial. Investigators previous to the writing of this paper, had found that the stillbirth and neonatal mortality-rates had decreased during the period of barbiturate administration. Some also found that the infants lost less weight and gained weight quicker when the labour had been conducted under analgesics. It has been suggested that the physiologic weight loss might be more than just physiologic and perhaps is a direct index of the amount of shock sustained. Apart from this amount of weight loss and the rate of weight loss recovery there was a tendency for the babies born under the influence of drugs

to maintain a more normal temperature for the first 10 days of life. These findings become all the more interesting when it is realized that the percentage of low forceps is high when the labour is conducted under some form of analgesia. One would expect an operative delivery itself to have a deleterious effect on the infant and that this might be enhanced by the analgesic used.

As the result of these accounts in the literature and of his own investigations the author is of the opinion that there is a high degree of general safety for the newborn when the mother is delivered under many of the modern varieties of pain-relief. He thinks that opiates are probably the only analgesics that may materially affect the infant adversely and may be particularly hazardous in cases of prematurity.

A SKIN TEST FOR THE DIAGNOSIS OF PREGNANCY

As skin reactions have been used as an aid to clinical diagnosis of many conditions the authors were of the opinion that a skin reaction to some antigen might be obtained to distinguish pregnant and non-pregnant individuals. One of them had extracted a protein from the placenta many years ago but it was not satisfactory because of the difficulty in getting it sufficiently refined. Since then other workers have made placental extractions but the intradermal reaction was positive in only 75 per cent of pregnant women but negative in the non pregnant. In this paper they describe their results after the injection of colostrum into the skin. The material was obtained by expression after cleansing the nipple with ether and it was diluted with an equal amount of sterile normal saline solution. The injection was made into the flexor surface of the forearm and a weal was formed by injecting exactly 1/50 of a c.c. A similar sized weal was made with physiological salt solution a few inches lower as a control. After about 30 minutes the weal would appear pearly with little or no pinkish areola around it if the patient was pregnant. If the patient was not pregnant the weal would remain pearly for a few minutes and then would begin to increase in size eventually

becoming two or three times the size originally produced by the injection, without changing in colour. Then there would appear a pinkish-red areola, one or two inches in diameter, which was irregular in contour and in depth of colour. This reaction would grow in intensity for an hour and persist for four or five hours.

The authors injected 265 known pregnant women in various stages of pregnancy, 358 known non-pregnant cases, including adult males, children, menstruating women, normal non-pregnant women, and women with known gynaecological abnormalities and 50 unknown problem cases to establish diagnosis. Of the 265 known pregnant women there were five false reactions. Two non-pregnant reactions were obtained one of which later gave the reaction for pregnancy and the other was not repeated. Three weak non-pregnant reactions were also obtained but disappeared after an hour, contrary to the usual non-pregnant reaction. It was also found that very early in pregnancy and during labour that there was a tendency to get a weak non-pregnant reaction which did not persist. Of the 113 known non-pregnant females, four cases gave a typical pregnant reaction. These were all in the menopause not having menstruated for five to 17 years. Of 50 post-partum cases varying from two to eight weeks after delivery all but three gave a non-pregnant reaction. Thus the test was correct in 98 per cent of pregnant women and in 96 per cent of non-pregnant women. Children before puberty reacted similarly to pregnant women.

From these experiments the authors came to the conclusion that the failure of the pregnant woman to react to the injection is due to an immune state which prevents the local reaction at the site of the injection. The weak reaction, seen in about 80 per cent of the cases in the first six and last three weeks of the pregnancy during labour and in the early days of the puerperium is the exception. The specific protein contained in colostrum from primiparous women is not contained in human milk or in colostrum or milk obtained from the cow, as no specific reactions were obtained with these substances.

REPORTS OF SOCIETIES

THE ROYAL ACADEMY OF MEDICINE IN IRELAND

A meeting of the Section of Obstetrics was held on Friday, November 20th 1942

Dr BETHEL SOLOMONS showed

A SPECIMEN OF PLACENTAL POLYPUS

The patient was aged 36 she had had 11 children, the last 11 months previously. She was admitted to the hospital in September 1942. She had nursed her baby menstruation has recommenced 4 months ago. Since July bleeding has been more or less continuous. Examination revealed a rather soft, slightly enlarged uterus. She was in such a collapsed state on admission that it was decided to give her a blood transfusion. As a temporary measure she was given intravenous saline and the uterus was plugged. Owing to her condition it was decided that conservative measures would be dangerous and total hysterectomy was done. The pathological report by Dr Bourke was as follows:

Tumour This is a simple placental polypus with necrotic chorionic villi all through it. At one or two places on the surface the villi appear to be covered with living cells. The endometrium in the roughened area above the polypus shows much blood in the interstitial tissue with large areas of hyaline degeneration around the blood-vessels. There is also evidence of early adenomyosis."

Dr BETHEL SOLOMONS said that when he got the report he believed the condition was very rare, in fact it was one of those conditions that he had taught about but had seldom seen. He could find no records as to its frequency. The appearance of the specimen which he showed was consistent with the description of Novak. He suggests that profuse haemorrhage may occur from rupture of the large venous sinuses at the base of the polypus and he recommends the pathologist to take care to make a differential diagnosis from chorionepithelioma. In this case no history could be obtained of a definite abortion nor of retained placenta at the last birth.

Dr D J CANNON showed

A CASE OF UTERINE PLACENTAL POLYPUS

which was associated with severe bleeding so severe that a blood transfusion had to be administered prior to operation. Curettage revealed normal endometrium. When the uterus was split after supra vaginal hysterectomy the appearance of the polypus so closely resembled that of a malignant polypus that he decided to remove the cervix and both ovaries. The patient made an uneventful recovery. The polypus showed microscopic evidence of chorionic villi.

Dr CANNON also showed

TWO FALLOPIAN TUBES ASSOCIATED WITH A CHOCOLATE CYST OF THE LEFT OVARY

The Fallopian tubes showed a deposit of fat globules and fatty acid crystals in the submucosa. This was apparently a metabolic change due to some unknown cause.

Dr JAMES QUINN showed

A SPECIMEN OF UNILATERAL CHRONIC SALPINGITIS

He said he considered it interesting as the size of the Fallopian tube was unusual, and the condition unilateral.

The patient was aged 51 a widow without children. She suffered from vague abdominal discomfort and evening rise of temperature. The symptoms were not acute but tenderness and pain were mainly referred to the back and left side. In spite of her age her periods were quite regular until about 6 months ago. She had 6 months of amenorrhoea of menopausal type and then had severe bleeding with clots which lasted 5 days. A large mass was felt on the left side of the abdomen, extending above the umbilicus. It was smooth and some mobility and tenderness were noted. Rectal examination revealed an impacted mass in Douglas's pouch. Further examination showed that the cervix had no signs of erosion or carcinoma.

matous change but there was a cystic mass in the right fornix. The uterus appeared to be enlarged. A diagnosis of ovarian cyst with possible fibroids was made and the abdomen was opened. Operation revealed a huge left pyosalpinx full of fluid and enormously distended. The uterus was enlarged and soft. The right Fallopian tube was merely thickened. The uterus was removed with both ovaries and Fallopian tubes, after having first removed the left Fallopian tube separately. Both ovaries were apparently normal. The vagina was left open for drainage. The pathologist reported 'a huge pyosalpinx filled with straight-forward polymorphonuclear pus'. The tubal condition was a chronic pyosalpinx and not tuberculous.

Dr QUINN went on to say that it is obviously not an acute condition; he did not know why a unilateral salpingitis of this nature should arise and would be interested to hear any comments on the matter. The uterus was large and thickened without any definite pathological condition other than that which one would associate with chronic congestion. The other Fallopian tube was thickened and hard, it contained no pus.

The PRESIDENT, DR NINIAN FALKNER, Master of the Rotunda Hospital, said they had all been interested to see these specimens with regard to the question of placental polypus; he thought the first unessential cause to be partly retained placental tissue following confinement. He thought it fairly common for part of a placenta to remain *in utero* without being recognized at the time. It may give rise to haemorrhage and during the treatment the placental tissue may be removed. A number of patients go through a period without undue loss and afterwards placental polypus develops. Chorionic tissue becomes absorbed but the blood-vessels at the base of the cotyledon seem to remain in the same position.

He said he would like Dr Solomons to say how long after delivery his patient came for treatment. Dr Cannon stressed the point of diagnosis at operation but surely diagnosis in these cases should be made not when the abdomen is opened but by curettage. It is quite easy as a rule to get a bit of the polypus and the presence of villi would disclose the diagnosis at once; the pathologist would have no difficulty in stating if the villi were

microscopically, those which are found in chorionepithelioma. He had very little to say about the condition of the Fallopian tubes in Dr Cannon's case, except that there is a great deal of fat in the corpus luteum. With reference to the chocolate cyst, he said he was not clear whether it was endometrium or cyst filled with blood.

Referring to Dr Quinn's specimen, the President said it was one of the largest Fallopian tubes he had ever seen. The only explanation as to its size is, that at the same time this Fallopian tube had become twisted and had a haemorrhage into it, which had gradually become absorbed; that supuration had taken place and when the Fallopian tube was removed all sign of haemorrhage had disappeared. Was the condition of the Fallopian tube recognized at the time of examination which would suggest that there had been a haemorrhage, and had there been a remote history of acute abdominal illness and recovery without operation?

Dr J. F. CUNNINGHAM said he had seen cases similar to those shown. The reason for the lack of statistics of placental polypus was that it was such a rare condition. He said he thought he had seen one case 5 months after delivery and went on to describe the symptoms and treatment he had given for the severe bleeding; he performed total hysterectomy and gave a blood transfusion. On examination the uterus was empty. There was a large sinus present.

Dr Cunningham said he was also interested in the large Fallopian tube shown by Dr Quinn. He had seen a case with a pelvic abscess; he opened Douglas's pouch but no pus was found. He felt a cystic mass and found the right Fallopian tube very distended; the left Fallopian tube was normal. He stated that it was hard to explain the condition of salpingitis. There were no adhesions in his case.

With reference to Dr Cannon's case he said he could not offer any explanation to account for fat globules being deposited there.

Dr J. O. E. APTHORP asked Dr Solomons and Dr Cannon did they not think the term uterine polypus wrong and misleading? Both cases showed evidence of actively growing tissue. If a bit of placenta is left behind it is no different from any other foreign body, therefore it is not actively

growing He suggested that the term should be changed

With regard to Dr Quin's case both Fallopian tubes showed chronic inflammation Would the end result depend on whether the Fallopian tube became sealed off Why should one become sealed off and one not?

Dr E SOLOMONS also spoke

Dr Bethel Solomons, in reply to various questions said if there was any doubt as to malignancy total hysterectomy should be done He suggested that polypus was a better word than polyps Curettings might easily be negative as they were in his case

The last baby was born 11 months previously the patient lactated for 7 months and then the bleeding started and was nearly continuous

Dr Cannon in reply to questions said that the uterus was curetted in his two cases and both were negative Therefore he considered it very difficult to make a diagnosis by curettage He treated the first case by supravaginal hysterectomy, the second case by total hysterectomy

There was according to Dr O Kelly no evidence of inflammation of the Fallopian tubes in the second case

Dr Quin also replied

Dr J F CUNNINGHAM read a paper

ON THE TREATMENT OF ECLAMPSIA

and reported 105 cases from the National Maternity Hospital He stressed the importance of attention to the condition of the kidneys the liver the cardiovascular system and the amount of oedema present He made special reference to the use of magnesium sulphate in treating eclampsia and produced figures showing a diminution in the mortality-rate and in the number of fits under this treatment He drew attention to the importance of an accurate history as a help in determining the presence of a previous lesion in any vital system He pointed out that most of the fatal cases occurred in those who had neglected prenatal care

The PRESIDENT thanked Dr Cunningham for bringing this communication before the Academy and remarked on the decreased mortality-rate of maternity cases He thought half the deaths were

due to the toxæmias of pregnancy He said that in the Dublin maternity hospitals there have been an average of 10 to 12 deaths in a period of 7 years from eclampsia Dr Cunningham's figures bore that out they also show that since the establishment of the routine use of magnesium sulphate and highly concentrated glucose solution combined with careful observation and nursing, the death rate from eclampsia would probably be reduced by 50 per cent He was interested to hear of the histories of the fatal cases and agreed with Dr Cunningham that if these cases had received antenatal care the result would have been different He congratulated him on the treatment of 105 cases of eclampsia and particularly on the results of the last 50 cases

Dr BETHEL SOLOMONS said he was glad to take this opportunity of paying tribute to the excellent work which Dr Cunningham had done for the Dublin School of Midwifery and for the National Maternity Hospital

The subject of eclampsia had always interested him and he had brought 204 cases with a mortality of 8 per cent treated during Dr Tweedy's mastership before the British Congress of Gynaecologists in Liverpool Of these cases 30 occurred during the last 2 years of the mastership when Dr Freeland and he were assistants when there was no mortality He thought it would add to the value of the excellent paper if in dealing with the 119 cases in the first series it were stated how many received prenatal care

Dr CORBET congratulated Dr Cunningham on his communication and congratulated him on the excellent results achieved in his last 50 cases He thought that the real significance in the treatment was not perhaps so much the reduction which appeared in the mortality rate but in the control of the fits, as shown by the very small percentage which occurred after treatment had started He agreed with Dr Cunningham on the importance of dehydration and had used this method since its publication by Fay and Arnold in 1932 He had used magnesium sulphate on only a few occasions as he had found great difficulty in obtaining the required solution in ampoules He did use, as long as he had been able to obtain it the 50 per cent solution of glucose for intravenous injection and

he did not find that it invariably caused a rise in blood-pressure although in some cases it certainly caused a rise in the tension of the cerebrospinal fluid

He used lumbar puncture almost as a routine, and was satisfied that some cases benefited greatly from it. One patient, who had haemoglobinuria, a sign which previous experience had always led him to believe of fatal import, showed immediate improvement on lumbar puncture and eventually recovered. He used venesection only when there were signs of embarrassment of the right heart occasionally in these cases a dramatic result was produced.

Dr Corbet quoted statistics compiled from collected hospital reports of English, Scottish and Colonial institutions. The totals for these institutions showed a variation in the incidence from 5.7 per cent of admissions for Trinidad to 0.3 per cent of admissions for Hong Kong. The mortality-rates varied from 16.3 per cent to 12 per cent.

The incidence-rate at the Coombe Hospital was 5.3 per cent and the total mortality-rate 12.5 per cent.

Dr QUIN congratulated Dr Cunningham on his results. In comparing his figures with previous Dublin figures, particularly Dr Tweedy's, it must not be forgotten, he said, that in those days there was a completely inadequate system of antenatal treatment, and therefore there must have been a number of patients who would never have developed eclampsia with our present antenatal treatment. Therefore the mortality statistics then would be actually less than now.

He asked Dr Cunningham about the value of lumbar puncture when cerebral symptoms were marked. He stated that he considered gas and oxygen anaesthesia an improvement on chloroform. With regard to gastric lavage, he looked on it as unnecessary.

Dr R. W. SHAW discussed the question of anaesthetics. He said he would like to ask Dr Cunningham if he was able to use pure gas and oxygen in these cases. It would appear that many of these cases must have been extremely difficult for any anaesthetic. In his experience he found even in emergency cases of abdominal section,

the administration of gas and oxygen alone a peculiarly difficult one unless the patient was adequately prepared. He also asked if Dr Cunningham considered that the administration of ether or chloroform definitely adds to the risk or whether he considered that if there is difficulty with gas and oxygen, it would be better to give a pure ether anaesthetic.

Dr A. W. SPAIN, Master of the National Maternity Hospital, said what impressed him most when he took up the mastership from Dr Cunningham, was the organization of the treatment of cases of eclampsia when they came into the hospital. He had no change to make and the treatment with magnesium sulphate was still used. It was too soon to give the number of cases of eclampsia since he took up the mastership, but it has been small, he had one in the first 6 months and then 7 or 8 cases. Dr Spain said he used gas and oxygen and found it ideal in cases of eclampsia. He had performed one Caesarean section under local anaesthesia. Three hours before the operation he thought the case was hopeless and at that stage did a lumbar puncture. She then showed some slight improvement and he did the Caesarean section.

Dr Spain said he hoped to continue Dr Cunningham's line of treatment with magnesium sulphate. He considered it would be better to avoid morphia.

Dr E. SOLOMONS congratulated Dr Cunningham on his results. He said he would like a few details about submammary, intravenous and intramuscular injections. Had he ever seen any bad results or any local bad effects follow such injections? He asked him if there was any scope for the use of magnesium sulphate in other severe toxæmias.

Dr F. Cunningham thanked the President and Section and the various speakers for the reception of this paper and the complimentary things said about it. He said he had studied Dr Tweedy's remarkable success in the treatment of eclampsia. He considered that the long distances which eclamptic patients had to travel by car nowadays had a very bad effect and that in Dr Tweedy's day long journeys by car were not so frequent. The same thing would apply to Dr Corbet's statistics.

As regards liver tests, he did the Vanden-

burg test only, as there is not time for others in acute eclampsia. The function of the kidneys is tested by estimation of the blood-urea. Magnesium sulphate is given early when the blood-pressure is inclined to rise, if given with the glucose it did not rise. He said he considered that magnesium sulphate, if given in the beginning, is a great help. Lumbar puncture was not done as a routine when one can give the patient a concentration of glucose. It is done in a patient in whom there is a good deal of restlessness and nasal itching, with good results, and when the patient gets strong solutions of glucose. The mortality rate in eclampsia depends

on the type of case whether they had had prenatal care or not.

He went on to say that there must be a place for Caesarean section in eclampsia but it was difficult to make up one's mind when a patient is in labour with eclampsia. The general results with Caesarean section were very bad.

Dr. Cunningham said he never gave any other anaesthetic but gas and oxygen. He gave a maximal dose of a quarter of a grain of morphia. No patient had more than 1 grain during 24 hours.

He gave injections intravenously and intramuscularly.

THE
Journal of Obstetrics & Gynaecology
of the British Empire

VOL 50, No 5

NEW SERIES

OCTOBER, 1943

Schistosomiasis (Bilharziasis) of the Female Genital Tract
and Neighbouring Tissues

BY

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Contributed from General Hospital, Salisbury, Southern Rhodesia

THE pathological changes constituting schistosomiasis or, as it is often called, Bilharziasis are produced by certain nematode worms of the family Schistosomidae. The adult forms of these worms generally exist in pairs and are found in the abdominal veins, including the portal system.

Bilharzial disease of the female genital tract is decidedly rare in temperate climates. As it is common in certain parts of the world, and as it affects other peoples in addition to the indigenous population it has been considered worth while drawing attention to this condition. With the increase of the European population in Africa there is reason to anticipate that such cases will be observed more frequently in Great Britain as a result of the periodic visits of the population to the homeland.

It is the purpose of this paper to deal with this disease from the gynaecological point of view, but as schistosomiasis is so seldom seen by gynaecologists in countries in which the disease does not naturally occur it will be better first to consider the general pathology of the disease at some length.

HISTORY

In 1851 T. Bilharz discovered the worm which causes epidemic haematuria in Egypt. It is often known as Bilharzia haematobia, but its international zoological name is *Schistosoma haematobium*. The ovum of the species described by Bilharz is provided with a sharp terminal spine which facilitates its movement through the tissues of the human host. A lateral spined ovum was discovered by P. Manson in 1903, in the West Indies. R. P. Leiper later showed this ovum with the lateral spine to belong to a different species of worm known as *Schistosoma Mansoni*. Both these varieties are common in many parts of Africa. In addition to these varieties a third has been described, the *Schistosoma japonicum*, which is found in the Far East. This organism was first described by Katasurada in 1904, in Japan. The ova of this variety are spineless.

Certain species of snail have been found to act as the intermediate hosts of the schistosomes. This discovery was first made in the case of the Japanese variety, by Fujinami and Nakamura. Some years later

R P Leiper, who was working in Egypt, showed that the miracidia, which are formed from the living ova deposited in water, entered and lived in a fresh-water snail called *Bullinus* and he subsequently showed that the miracidia developed from ova of *S. Mansoni* underwent further development in another fresh-water snail, *Planorbis*. In countries in which these diseases are endemic these snails are plentiful. Waters which contain *Bullinus* snails infest bathers with *S. haematobium*, while waters which contain *Planorbis* cause infection with *S. Mansoni*.

Other varieties of schistosome infection are known. One variety, *S. bovis* is found in sheep, another variety known as *S. intercalatum*, first found in the Belgian Congo, is described as possessing a terminal spine which is, however, longer than that of *S. haematobium* but shorter than that of *S. bovis*.*

MODE OF INFECTION

In all three common varieties of human schistosomiasis the infection is contracted by bathing or wading in water which contains infected snails. The fresh-water snails in which the organism develops are generally found in stagnant pools, as a rule sluggish waters are favourable to *Planorbis* snails, whereas *Bullinus* snails prefer a faster stream.

The infected urine or faeces is passed

* The animal schistosomidae include

S. bomfordi—Inhabits the portal system of Indian oxen. The male possesses 60 testicles.

S. spindale—Inhabits the portal system of Indian buffalo. The male is provided with 6 or 7 testicles.

S. indicum—Inhabits the portal system of Indian horses and camels.

S. turkestanicum—Inhabits oxen. The ova have spines at each pole.

S. matthei—Inhabits sheep, cattle and man. It resembles *S. bovis*.

into water or into wet soil and the living ova thus set free develop into free-swimming structures which are known as miracidia. These miracidia invade the body of a suitable mollusc host and pass through a part of the cycle of the life history of the schistosome inside its body. In due course the snail discharges enormous numbers of minute bodies, called cercariae, into the water in its vicinity. Human beings who bathe in water containing cercariae are invaded by these organisms which generally penetrate the skin. This is the usual method of infection but it is possible for infection to arise from drinking infected water, in this case the organisms enter the body through the mucous membranes of the mouth, pharynx or oesophagus. Children and young adults are the most common subjects because of their habit of bathing and paddling in streams and pools. Infection generally takes place very early in life. For this reason the earliest signs are rarely seen in the native, but they may be seen from time to time in the European child whose parents are more observant. The initial disturbances usually occur 3, 4 or more weeks after exposure to infection and they consist of general *uticaria*, *malaise*, and a slight rise of body temperature. In due course the worms reach maturity in the human body and according to the organs in which the eggs are deposited so do the symptoms vary.

It is well to point out here that acute dermatitis resulting from the penetration of the skin by cercariae of a schistosome is not limited to the geographical distribution of *S. haematobium*, *mansoni* and *japonicum*. Cercarial dermatitis has recently been studied in America because it has been found to be common among bathers in Michigan, Wisconsin and Manitoba. The condition has also been described by Matheson as occurring in the British Isles, namely at Cardiff. Cort has described his

own sensations after immersing his hand in water infested with cercariae. About 10 minutes after immersion a prickly sensation is felt and this is quickly followed by urticarial blotches which subside after about half an hour, leaving numerous macules. Within 24 hours itching becomes intense and papules appear, in 2 days the hand becomes swollen, painful, and the papules become pustular. The condition subsided in 5 days. It was noticed that the horny skin was not affected, the cercariae appeared to make their entry through the hair follicles.

The cercariae first identified by Cort as causing bather's itch were *C. elvae* Miller. Those occurring in Cardiff were *C. ocellata*, which appears to be the common schistosome in European outbreaks of bather's itch. Cort considers that most of the 20 odd cercariae such as *C. douthitti*, *C. physellae* and *C. stagnicolae*, which do not cause systemic disease in man, are capable of causing dermatitis. The possibility that one or other of these cercariae might develop the ability to invade the human body like the cercariae of *S. haematobium* would be alarming in view of their wide distribution. As in the case of cercariae which cause systemic disease in man the intermediate hosts are water snails either *Lymnaeidae* or *Physidae*. The carrier snail of Cardiff is *Lymnaea stagnalis*.

Not much is known about the adult schistosomes, but it is believed that they are to be found in certain varieties of water-bird. One of the cercariae, *C. douthitti*, is known to be derived from a schistosome which infects mice, musk rats, guinea pigs and rabbits.

Microscopical examination of skin exposed to cercarial infection has shown the absence of parasites of bather's itch in specimens taken up to 50 hours after infection. Sections show numerous burrows, some of them blind, which do not extend

deeper than the Malpighian layer. It would appear that evidence has not been submitted to date which indicates that systemic infection occurs from these common cercariae of temperate climates, but it should be borne in mind that such infection is a possibility. Penner immersed a young Rhesus monkey in water containing large numbers of *C. douthitti* and at necropsy nearly 6 days later found plentiful worms in the lungs. It is therefore possible for the same process to occur in man.

Man is infected by the pathogenic schistosomes in two ways: (1) exposure of the surface of the body to infected water, (2) exposure of a mucous membrane to infected water, e.g., by drinking. The skin route is the more important mode of infection. Drinking water which contains cercariae is also capable of producing systemic infection, in this case the cercariae adhere to the mucous membrane while passing through the mouth, pharynx and oesophagus, by means of their suckers. Infection through the stomach is not possible because the cercariae are killed by the acidity of the normal gastric juice.

All schistomulæ enter the definitive mammalian host through the skin or mucous membranes to reach the blood-vessels or lymphatics. Having penetrated the body of the mammalian host they lose their tails and passing through the vessels they reach the right heart, the pulmonary vessels, the lungs, the left heart, and thence they pass to the general circulation. Their main route is from the lungs to the liver through the arterial circulation, and through the gastro-intestinal vessels to the portal and mesenteric veins. During the next 6 weeks they develop into adult worms, the adult worms migrate to most of the large abdominal veins, the exact distribution varying according to the species. After copulation the female is believed to pass towards the smallest veins,

where she deposits her eggs, but the usual course for the male with the female in his gynaecophoric groove is to pass on until arrested in sub-mucous tissues which, in the case of *S. haematobium*, are those of the genito-urinary tract generally and the bladder in particular. The bladder seems to be the normal goal of mature worms and most eggs are deposited there. Unusual tumours of *S. haematobium* origin may be found about the bladder, in the broad ligament and in the skin, these contain many eggs which have been deposited by worms which have wandered the wrong way.

Congenital infection

It would appear that infection may be congenital. Narabayashi has observed ova of *S. japonicum* in the stools of three newly-born infants whose mothers had been working during their pregnancy in contaminated rice fields. Fujinami, Nakamura and Narabayashi have also observed the infection of the foetus of dogs and guinea pigs. The significance of these observations is that the cercariae or the young worms are capable of traversing the placenta.

DISTRIBUTION OF SCHISTOSOMIASIS IN EUROPE

Some cases of schistosomiasis have been reported in Portugal in people who had never been out of the country. The intermediate host is believed to be *P. corneus*. In most of the cases recorded in England the disease was contracted in Africa or elsewhere, but one case has been described in an Englishwoman who had never left the Erith-Gravesend district.

IMPORTATION OF INFECTED DEFINITIVE MAMMALIAN HOSTS

Schistosomiasis occasionally extends beyond its endemic areas. Certain areas

of the Sudan have become heavily infected owing to the importation of Egyptian labourers. It has also been suggested that the disease will become endemic in the south of France owing to the local presence of *Bullinus* snails and colonial troops, especially Senegalese troops.

MORPHOLOGY

The schistosomes which are common in Africa are *S. haematobium* and *S. mansoni*. In each case there are male and female worms. The male of *S. haematobium* is about 1.5 cm long and 1 mm in breadth. The male of *S. Mansoni* is about 1 cm in length and 1 mm broad. The male of *S. japonicum* is even smaller. All the male worms are flat and have thin lateral extensions which are capable of being folded medially towards the ventral surface and by this means they constitute the gynaecophoric canal. The lateral folds are provided with numerous tubercles with which the female is grasped.

The female worms differ from the males in being round and in being longer than the males. The female of *S. haematobium* is 2 cm long, and the female of *S. Mansoni* is about 1.5 cm long.

The uterus of *S. haematobium* produces a large number of ova provided with terminal spines while the uterus of *S. mansoni* is characterized by containing very few lateral spined ova, generally one to three in number.

In order that they may adhere to the inner lining of veins, both the male and the female are provided with two suckers attached to the ventral surface at the anterior end.

When the ova of these organisms are deposited in water the containing shell ruptures as a result of the change in osmotic pressure and a free-swimming embryo is set free. These small structures

are known as miracidia. They live for about one or two days and during this time search for the appropriate snail. When a snail of the proper species is found they penetrate its body through the antennae or the skin in the region of the neck.

In the body of the snail they develop into sporocysts which in their turn give origin to daughter sporocysts, the latter are branching bodies capable of slow movement. Most of the sporocysts reach the liver of the snail where, in a period of 5 to 6 weeks, from the time of the initial snail infection, they give origin to very large numbers of cercariae. The cercariae are capable of boring through the tissues of the host and, reaching the pulmonary system, are ejected into the water about the snail.

These cercariae swim freely in the water, and provided the water is reasonably warm are capable of living for about 36 hours. Within this time they must find a suitable host, namely, man, rats, mice, monkeys, guinea pigs, or perish. It is possible to see the cercariae with the naked eye, they appear as thin white threads in the water. In the case of *S. haematobium* the cercariae are about 400 microns long.

Fate of the eggs in man

During their journey through the tissues, the shells of the eggs become thicker and yellower, and the egg doubles its size until it becomes about 140 microns long by about 50 microns broad. While in transit through the human tissues a miracidium develops within the shell and by the time they are voided in the urine or faeces they are generally well developed. Should an ovum fail to make its way into a viscus the miracidium dies, the shell shrinks and the contents calcify. These dead structures stimulate the formation of much local connective tissue. Sometimes such dead ova

are afterwards set free and appear in the excreta.

Length of life of schistosoma in man

It has been estimated that the worms are capable of living for as long as 30 years in the vessels of man. During this time they produce millions of ova. Rameses Girges records one of his cases which was found to be passing living ova 26 years after the original diagnosis had been made. There is always the possibility of re-infection in persons normally resident in areas in which the disease is endemic. However, Christopherson mentions the case of a physician who was infected with schistosomiasis who, 28 years after his return to England, was still passing living ova in the urine.

GENERAL PATHOLOGY IN MAN

The initial lesions of schistosomiasis are rarely seen in the indigenous native, but they are sometimes seen in Europeans residing in endemic areas. The earliest indications of infection are urticarial blotches (the Baoonah itch of Girges), malaise and mild pyrexia. The adult worms are found in man about 6 weeks from the time of infection, they live in the large venous sinuses of the urinary and lower intestinal tracts. The eggs of these organisms have been found in the lungs, the gall bladder, the appendix, the spinal cord and other places. When these worms are present in man there is a considerable blood eosinophilia.

The lesions caused by *S. haematobium* and *S. Mansoni* are much the same. *S. haematobium* worms live in both the urinary and intestinal tracts and the ova may be found in both urine and faeces. Every part of the genito-urinary system may be implicated in varying degrees, the worms being distributed throughout the pelvic plexuses, vesical, prostatic and

uterine *S. Mansoni* lives in the large vessels of the portal system, especially the superior and inferior mesenteric veins and their tributaries. The worms have a natural tropism towards the venules of the large intestine.

The tissue changes produced by the passage of ova through them are essentially very slow and chronic. Tissue eosinophilia is marked and fibrosis may be extreme.

In the past it has been the custom to divide Bilharzial lesions into two types, namely, the hypertrophic and atrophic. This division is arbitrary, both types of lesion often existing side by side, this subdivision does not really serve any useful purpose.

The hypertrophic variety of lesion is characterized by marked proliferation, particularly of epithelial cells, these changes give origin to papillomatous growths. The second or atrophic variety is caused by the development of massive, dense, fibrous tissue. The hypertrophic form, therefore, represents the reaction to the disease of epithelial covered surfaces such as the lining of the urinary and intestinal tracts. The connective tissues of the body are the true seats of the so-called atrophic lesions. In those places where the anatomical arrangements are suitable a mucous membrane may show papillary formation and the neighbouring connective tissues may be extremely thick and as hard as leather. This condition is sometimes seen in connexion with the ascending colon which is essentially a retroperitoneal organ and also in the broad ligament in relation to the Fallopian tube.

All these changes have been described from the kidney substance to the external urinary meatus and from the stomach to the anal canal and orifice. The distribution of the disease in the female genital tract and the perineum is the purpose of this paper. It is well known that the

genital tract of the male is frequently infested by Bilharzia, but little attention has been paid to the distribution of this disease in the female.

The close proximity of the bladder, the lower ends of the ureters and the urethra to the genital apparatus is of such importance in connexion with Bilharziasis of the female organs that it is worth while passing in brief review the pathological changes which may be observed in these structures as a result of Bilharzial infection.

1 *Local hyperaemia*

The first change produced in the tissues is engorgement of the vessels and this is associated with oedema. The swollen area is soft to the touch and has an appearance much like that of velvet. The centre of such an area is often dusky purple in colour while the edges are dull red. In both the bowel and the urinary tract these areas are often covered with mucus. Between areas of this nature, which may be numerous, areas of relative pallor are to be found. Here and there in these pallid areas one may observe minute granules which lie deep to the epithelium. Tissues affected in this way have been described by the earlier writers as resembling tissues in which sand has been scattered, this is, as a matter of fact, a good description of the appearance of these patches. It will be appreciated that the soft vascular areas mentioned above are liable to bleed on the most minor injuries.

Pieces of tissue such as those just described reveal the presence of Bilharzial ova when submitted to microscopic section and the eggs can sometimes be found in a smear taken from the affected tissue.

2 *The "sandy patches"*

The patches with an appearance like that of scattered sand would seem to form

rapidly after the local areas of hyperaemia and it is highly probable that the hyperaemic patches turn into the sandy variety with the passage of time. The sandy patches are variable in size and shape, they are of a yellowish colour and are deep to the epithelium. Close examination reveals that they are made up of minute granules. In many ways the appearance of these patches is much like that of the so-called "strawberry" gall-bladder with its small sub-epithelial deposits of cholesterol. After a time the sub-epithelial tissues become infiltrated with increasing amounts of fibrous tissue and the affected area becomes harder. Some areas may become partially calcified.

3 *Local interstitial haemorrhage*

In some early cases sub-epithelial haemorrhage may be present. This would appear to be derived from the initial hyperaemia, the dilated vessels either being traumatized or otherwise injured by the passage of ova.

4 *Bullous oedema*

In other cases bullae may be found arising from the mucous membranes. Such bullae may contain clear, turbid or haemorrhagic fluid. The neighbouring tissues are generally oedematous. In the urinary tract they are fairly common in the vicinity of the ureteric orifice.

5 *Papilliferous changes*

Neoplastic changes are fairly common in mucous membranes affected with this disease. The usual form of new growth is the papilloma which may be of the sessile or long filiform variety. They have the same structure as ordinary papillomata. The adult worms are occasionally seen in the vessels towards the base of a papilloma. The papillomata are usually infiltrated with the cells characteristic of

chronic inflammation and numerous ova may also be present. The filiform variety of papilloma generally traumatize each other and the epithelial surface is therefore often ulcerated and it bleeds freely.

6 *Ulceration*

Ulcers may arise in areas which have been the seat of great oedema, in the sandy patches, from the rupture of bullae and from the separation of papilliferous masses. Ulceration may also arise in epithelium with a deficient blood supply due to the fact that the subepithelial tissue is fibrosed.

Ulceration is rather more common in the bowel than in the urinary tract, presumably because of the frequency of secondary infection.

7 *Fibrosis*

All tissues invaded by Bilharzial ova become the seat of a slowly progressive chronic inflammatory reaction. Fibroblasts are produced in such numbers that the affected tissue becomes as hard as leather. Several authors have drawn attention to the fact that the sclerosis is sometimes so great that the tissue resembles scirrhous carcinoma, with ova lying between the fibrous bands in a manner similar to the malignant cells in, for instance, the so-called "leather bottle" stomach.

The changes described above are essentially those which can be observed in those organs which are provided with a lining of mucous membrane, but with the passage of time the changes go further than this. At the same time as the epithelial changes are taking place the muscular wall of organs such as the bladder, ureters and bowel are also affected. Many authors have drawn attention to massive diffuse infiltration of the meso-caecum, meso-appendix, meso-colon and meso-rectum, and from this it is clear that finally the

neighbouring connective tissue is affected. A similar change is found in the connective tissues of the broad ligament but little attention would appear to have been given to this.

It will be appreciated that the pathological changes recorded above really constitute a continuous picture which is slowly progressive in the direction of extreme fibrosis. One frequently finds several of the lesions which have been described existing side by side and no practical good can be expected from the classification except to provide one with a general knowledge of the individual changes.

It is important at this stage to mention that carcinoma may arise in or in the near vicinity of chronic Bilharzial lesions. The incidence of malignant disease in Bilharzial tissues appears to differ widely in different parts of Africa. It is encountered more frequently in Egypt than in other places and even here Girges found the incidence to be only a quarter of one per cent. Most of the cases diagnosed as carcinoma are really swellings formed by masses of schistosomiasis tissue.

BILHARZIASIS OF THE FEMALE GENITO-URINARY TRACT

As the genital and urinary apparatus are so intimately connected both developmentally and anatomically, and as infection of the one is so often connected with infection of the other it will be helpful first to describe the recognized changes in the lower urinary organs.

1. *The bladder*

This organ is a common site of infection with *S. haematobium*. All the changes described above are frequently found in the mucous membrane and sub-epithelial tissue of the bladder. As time goes on the bladder wall becomes more and more

infiltrated with ova, small round cells, eosinophils and fibroblasts and it becomes very hard and thick. In some cases it may be palpated above the level of the symphysis pubis as a hard mass, often of irregular outline. Some observers have described these hard bladders as reaching up to the level of the umbilicus, such cases have been found chiefly in Egypt. Calcium salts are sometimes laid down in the wall, in rare cases practically the whole wall is affected in this way.

The pre-vesical tissue becomes dense and fibrous and much of the mass which can be palpated is probably due to the chronic inflammation of the connective tissues. The normal loose connective tissue about the bladder becomes very thick and a similar change may also take place in the structures of the lower abdominal wall. In these cases the sensation given to the palpating hand is much like that of a diffuse carcinoma of the breast. Although the change may take place in any of the connective tissues about the bladder the usual site of the change is anteriorly whence it spreads into the abdominal wall. Spread in other directions is of great gynaecological interest. Fistulous tracks and sinuses are often present in the lower abdominal wall. More often than not these tracks are circuitous and frequently branch. They run in the planes between the peritoneum and the muscular wall and between the individual muscle planes. When traced at operation, or at necropsy, they are found to lead to masses of degenerate tissue which are generally placed round the upper part of the bladder and in the pre-vesical and lateral vesical tissues. Some observers have believed infections of this kind to take their origin in the loose pre-vesical tissues and spread thence to the umbilicus along the path of the urachus and possibly too along the lines of the obliterated hypogastric arteries.

2 *The urethra*

It has always been considered that the male urethra is far more commonly affected than that of the female, but so far as the true incidence is concerned one must remember that the female is less commonly affected than the male. In the female Bilharzial disease is generally an extension of vesical Bilharziasis. The local pathological changes are the same as those described above. The commonest clinical findings are thickening and ulceration of the mucous membrane and the formation of small papillomata. In addition to these changes peri-urethral abscesses are sometimes seen and these often give rise to urethral fistulae and discharging sinuses.

The local thickening in urethral Bilharziasis feels like that resulting from extensive infiltration of the anterior vaginal wall which is found in many advanced cases of carcinoma of the cervix uteri.

Small Bilharzial papillomata may be found emerging from the external urinary meatus when they may be mistaken for the ordinary form of urethral caruncle. Whereas the true caruncle arises from the gland-bearing area on the posterior lip of the urethra, Bilharzial hyperaemia and papillomata may be found arising from any part of the circumference of the meatus.

3 *The ureters*

The ureters are unfortunately often the seat of Bilharziasis, they demonstrate all the changes which have been described. Ureteral and peri-ureteral fibrosis is apt to be patchy, but it is most marked in that part of the course of the ureter below the level of the pelvic brim. Bilharzial strictures an inch or more above the entry of the ureters into the bladder often call for surgical interference. The ureter normally passes through fairly loose connective

tissue, but this is converted into tissue which is stony hard in Bilharziasis.

Every gynaecologist is familiar with the difficulties which may be encountered in the dissection of the ureters in Wertheim's operation, and he will therefore appreciate the special difficulty in exposing the ureters in the presence of Bilharzial disease in which the tissues are many more times thicker, harder and more extensive than in all but the most exceptional cases of carcinoma. One will also be able to form some idea of the nature of the tissues constituting the broad ligament particularly of that part normally traversed by the ureter.

THE GENITAL ORGANS

1 *The ovary*

There are few references in the literature to Bilharzial disease of the ovaries. Symmers in 1906 described a case in a young child. He noticed a mass of fibrous tissue which involved the upper edge of the broad ligament and the ovary. The microscope revealed the presence of Bilharzial ova in the ovarian substance. This case is cited again and again in the literature. There would seem to be little references to cases in which primary Bilharziasis is more definite than in Symmers' case. Rameses Girges states that the ovaries become scarred and fibrous and contain large numbers of Bilharzia ova in the parenchyma. They may be covered with a thick fibrous coat making ovulation impossible and thus lead to sterility. In several of the cases seen, and operated upon by the writer, ovarian Bilharziasis has been discovered associated with other genital lesions. The chance of finding Bilharzia ova in the ovary alone are very small, indeed there is really little interest in finding primary ovarian Bilharziasis in view of the fact that ova are also probably present in other tissues.

2 The Fallopian tube

The literature on tubal Bilharziasis is small. A case has recently been described from Johannesburg in which the distal part of the Fallopian tube was greatly thickened and the mesosalpinx was filled with hard masses of fibrous tissue. On section the Fallopian tube and adjacent broad ligament were found to contain numerous ova. In this case the tubal changes had caused the arrest of a fertilized ovum. The subject of tubal pregnancy in association with Bilharziasis is discussed below.

In 1941 Gelfand drew attention to two cases in an article dealing with the clinical features of Bilharzia Salpingitis. An outline of his cases is given below.

CASE 1

The patient was a married European aged 21 who originally consulted her doctor because of lower abdominal pain and amenorrhoea. She was found to be pregnant. She had a normal labour and was well for the next two years when she complained of sub-umbilical pain and backache. Neither leucorrhoea nor menstrual abnormalities were present. The patient, however, suffered from dyspareunia. Vaginal examination revealed the presence of a right tubo-ovarian mass. At operation a diseased Fallopian tube was found on the right side. The left Fallopian tube presented a few tubercles in its serous coat but otherwise appeared normal. To the naked eye the ovaries and uterus appeared to be normal. Histological examination of the Fallopian tube proved the diagnosis of Bilharziasis. A course of antimony was prescribed. About 2 years later the patient again became pregnant. The special interest of this is that although tubercles were found in the left Fallopian tube at operation the infection was not sufficiently severe to prevent the normal passage of the fertilized ovum. The course of antimony may have had something to do with this.

In connexion with this case record it is to be noted that no mention is made of the specific type of schistosomal infec-

tion of the Fallopian tubes, and as there is no mention of the result of urinary examination it is not clear whether this case is to be regarded as one of infection by *S. haematobium* or *S. Mansonii*.

CASE 2

The patient was an unmarried native aged about 19 years. She was admitted to hospital complaining of severe lower abdominal pains of a few days' duration. The temperature on admission was 101 F and the pulse rate 96. So far as could be ascertained she did not suffer from any menstrual irregularity, nor from leucorrhoea. On opening the abdomen the right Fallopian tube and ovary were found to be the seat of Bilharzial disease; the left Fallopian tube was apparently normal. The diagnosis of Bilharziasis was confirmed by histological study.

So far as this case is concerned no mention is made of the specific type of Bilharzial disease affecting the tube.

The cases which the writer has observed have always been found accompanied by considerable involvement of the broad ligament. The following are examples of Bilharziasis of the Fallopian tubes occurring in native women. In many cases it is difficult to obtain a satisfactory history as few native females speak English and none of them know their age.

CASE 1

No. 4066. Adult female, age estimated at about 25 years. This patient had been married about 5 years; she had never been pregnant. The chief complaints were low lumbar and sacral backache which had been present for about 3 years, and hypogastric pain which had started a few days before admission. The temperature was 101 F and the pulse rate was 110. The patient was not aware that she had ever suffered from Bilharziasis; the condition is well known to the local native under the name of "chifungwa". Menstrual abnormality had not been noted; the duration of the menses being about 5 days and they recurred at intervals.

of about a month. There was not any urinary disturbance.

On examination the patient was found to be thin but not anaemic. A mass could be felt on deep palpation above the symphysis pubis. Vaginal examination revealed the presence of a mass which was fairly hard in the pouch of Douglas.

On opening the abdomen bilateral tubo-ovarian masses were exposed. They completely obliterated the pouch of Douglas. Numerous loops of small bowel were adherent to the summit of these masses. They were freed by gauze and digital dissection when it was possible to see that the mass on the left was larger than the mass on the right. The enlarged ovary of each side was hidden below the corresponding Fallopian tube and covered by masses of fine adhesions connecting these structures to the rectum and lateral wall of the pelvis. The broad ligament and mesosalpinx of each side were very thick and peculiarly resilient. The masses were dissected free with gauze, the fingers and the scissors. During this manoeuvre several cystic spaces containing brownish fluid were inadvertently opened. Some of these appeared to be chronically inflamed massive follicles while others appeared to be false spaces derived from peritoneal adhesions. The diseased tissues were removed but a small piece of the right ovary which appeared to be reasonably normal was conserved. Separation of the left mass exposed an oozing area of pelvic wall which was devoid of peritoneum. The lower part of the posterior surface of the uterus was in a similar condition. In performing this removal one was particularly impressed by the gross thickening of the broad ligaments. A gauze and rubber tube drain were inserted in the usual way and the abdomen was closed. The patient made an uninterrupted recovery.

The pathologist's report on the specimen was as follows:

Morbid anatomy. Both Fallopian tubes are greatly enlarged and thickened, one to many times its normal dimensions. On cross section the increase in size is seen to be due to fibrosis of all layers. Conglomerate tubercles are not present. One ovary is much increased in size and the seat of several cysts. The other ovary contains a large cyst of follicular origin and is the seat of chronic inflammation.

On digestion the ova of *S. haematobium* was found.

Histology. There is well-marked chronic inflammation in both Fallopian tubes and ovaries. Eosinophils are abundant. While no typical Bilharzial tubercles are seen there is no doubt as to the cause, in view of finding the ova of *S. haematobium* on digestion.

Diagnosis. Chronic Bilharzial salpingo-oophoritis.

The digestion of the tissues mentioned above is carried out with 10 per cent caustic potash.

The urine examined on one occasion did not reveal the presence of any ova. This however is not sufficient evidence to exclude urinary Bilharziasis.

CASE 2

No. 412. Adult native female, age estimated at about 35 years. This patient complained of low abdominal pain which had been present for some months. It was impossible to elicit any medical history concerning the nature of the menses or of Bilharzial infection. The lower abdomen was peculiarly boggy to the touch. A definite mass could not be palpated. Bimanual examination revealed the presence of a fairly hard mass lying to the left of the uterus and displacing this organ to the right.

The abdomen was explored through a midline sub-umbilical incision. Difficulty was encountered in finding the peritoneal cavity because of adhesive bands between loops of intestines, the abdominal wall and the genital organs. The universality of adhesions was one of the most striking features of this case.

The adhesions and loops of bowel were dissected free and it was then possible to remove a ragged tubo-ovarian mass about the size of an orange. In applying the forceps to the structures containing the blood-vessels supplying the mass, the infundibulo-pelvic ligament was found to be so voluminous that only the largest Kocher's forceps could be applied to it directly. The abdomen was closed without drainage. The convalescence was uneventful.

Pathologist's report

An irregular tubo-ovarian mass, thick and hard to the touch. Conglomerate tubercles are not to be seen. A cyst is present inside the ovary.

Histology The cyst is derived from a Graafian follicle. Bilharzial tubercles are not present in the ovary but chronic inflammatory reaction is extensive. The Fallopian tube shows abundant tissue eosinophils and chronic fibrosis.

On digestion numerous ova of *S. haematobium* were found.

Diagnosis Chronic Bilharzial salpingo oophoritis. Examination of the urine showed the presence of the ova of *S. haematobium*. The stools were examined twice. ova were not found.

Six cases of a nature similar to those recorded above have been encountered during the course of the last year, the most noticeable features being the presence of dense and massive adhesions, the involvement of both the Fallopian tube and ovary of one or both sides, the extreme thickening of the broad ligament, the meso-salpinx and infundibulo-pelvic ligaments and the rarity of naked-eye changes in the uterus itself. The thickening and hardness of the tissues are such as are never encountered in any inflammatory condition of the pelvis found in temperate climates.

The nature of schistosomal disease of the Fallopian tubes would lead one to suspect that it is a fairly common cause of arrest of a fertilized ovum in the Fallopian tube. This, in fact, is true. In the Johannesburg case mentioned above the changes in the Fallopian tube, as a result of the presence of eggs, were sufficient to cause the arrest of the fertilized ovum. The following case was recently operated upon by the writer.

The patient was a well-educated native woman of 30 years who stated that 6 years previously she had taken a course of antimony injections for urinary Bilharziasis. Tests of cure had not, however, been carried out. This patient arrived at the hospital and stated that she knew she had an ectopic pregnancy in her right Fallopian tube. On being asked how she knew this she divulged that 4 years previously she had had similar pain on her left side

and the surgeon had removed her left Fallopian tube which contained an embryo. The patient's last period occurred about 6 weeks before the onset of pain in the right iliac fossa. Bleeding was not taking place from the uterus. The usual examinations were performed and a very tender mass could be palpated in the right Fallopian tube. At operation the diagnosis of right tubal pregnancy was confirmed and the Fallopian tube was removed. It was noted that the left Fallopian tube had been removed at the previous operation. Other evidence of local Bilharziasis could not be seen. The specimen was sent for pathological investigation. On examination of several sections no definite evidence of Bilharzial infection was seen but digestion of the Fallopian tube revealed the presence of the ova of *S. haematobium*.

This case is, therefore, one of ectopic tubal pregnancy due to schistosomal salpingitis and it is highly likely that the previous ectopic pregnancy in this patient was of the same origin. One also learns that the ordinary histological section of such specimens is not particularly helpful in establishing the diagnosis. The ova are often so few in number that the chances of finding them in the section are very small. Digestion of the tissue with caustic potash is an essential part of the pathological examination.

Tubal pregnancy associated with tubal schistosomiasis also occurs in the European. The following details have been provided by Mr R. M. Honey, F.R.C.S., in whose practice the case occurred.

The patient came to Rhodesia in 1937 at the age of 23 years. In the same year she went on a camping trip throughout which she used water from streams for all purposes. The waters in the district in which the holiday was spent are known to be infected with pathogenic cercariae. She married in 1938. At the end of 1939 she consulted her medical adviser as conception had not taken place. Examination revealed that the right Fallopian tube was obstructed.

The menses had always been within normal limits the loss lasting 5 to 6 days. The patient

had always suffered from dysmenorrhoea which was limited to the first and second days of the loss. After leaving hospital the characteristics of the menstrual cycle remained the same but the patient noticed that the first-day pains were becoming more severe. During this time the general health was good and her only complaint was that there was no sign of a family. The dysmenorrhoea gradually became worse, most of the pain being localized to the right iliac fossa. In August 1940 the patient began to lose weight and to feel very listless and minor efforts such as coughing or sneezing caused pain. The pain became worse and it was present continually in the interval between the menses.

The menstrual period which should have taken place at the end of September was missed. On October 13th there was a loss of blood *per vaginam* and several large pieces of tissue were passed. On October 25th as the loss had not ceased she consulted her doctor and was admitted to hospital. She was discharged after 5 days. During the next 3 weeks there was a slight loss of blood after which it ceased.

On December 15th the patient experienced a sudden violent attack of pain in the right iliac fossa; this was accompanied by vomiting and severe headache. The abdomen was opened by Mr Honey who discovered a right tubal pregnancy. The usual operation was performed; the convalescence was uneventful. The specimen was examined pathologically when the ova of *S. haematobium* were discovered. After recovery the patient was given a course of antimony injections since when her health has been satisfactory.

This European case demonstrates certain clinical points very clearly, they are (1) The patients rarely recognize that they have been infected. (2) Dysmenorrhoea tends to be of increasing severity, and the pain of tubal disease eventually becomes continuous during the menstrual interval. (3) Sterility. (4) The lack of upset of the menstrual loss and cycle. (5) The occurrence of ectopic pregnancy. (6) The general malaise which accompanies the established disease. All these points are mentioned more fully in the

section concerned with the clinical aspects of Bilharziasis in the female.

3 *The uterus*

In this country not any cases of Bilharziasis of the endometrium have been described in spite of the examination of numerous curettings and other specimens. The uterus as a whole is not commonly affected by the disease, but myometrial and endometrial schistosomiasis may be expected to be more readily detected when specimens are subjected to maceration and digestion with caustic potash. It has already been pointed out that the chances of finding an ovum in the tissues are very small in all except the most grossly affected tissues and it follows that when Bilharzial endometritis is suspected the best pathological examination to carry out is digestion of the specimen and not the preparation of a section in the usual way.

Bilharzial ova have been found in at least one specimen of myometrium subjected to digestion. The morbid anatomical changes of severe Bilharziasis of the myometrium do not appear to have been described.

Fibroids In the presence of severe schistosomiasis one might expect to find eggs in the substance of fibroids. In this laboratory eggs have never been seen in histological sections of fibroids, but they have been obtained from macerated fibroid tissue.

Endometrium Eggs have been discovered in the endometrium on at least three occasions, two of which were described by te Groen.

4 *The cervix*

Bilharzial disease of the cervix has been described on several occasions, but to date no such cases have been placed on written record in this country. Bil-

harzial ulcers and polypi have been recorded elsewhere as involving the vaginal part of the cervix and as high up the canal as the internal os. In the cases which have been described there would appear to be an accompanying Bilharziasis of the vaginal fornices and it may be that the disease reaches the cervix from the vaginal plexus of veins. Some authors have drawn attention to the similarity between Bilharzial disease of the cervix and carcinoma so far as their clinical appearance is concerned. There does not seem to be any literature on the possible association between cervical Bilharziasis and cervical carcinoma.

Madden has described the occurrence of small cervical fibroadenomatous tumours which contain multiple ova.

5 *The vagina*

Schistosomiasis of the vagina is not uncommon. It may be a 'primary' infection or spread from the base of an infected bladder or urethra. The fornices seem to be more commonly affected than does the lower part of the vagina and it seems probable that this is due in some measure at least to its anatomical relation to the inferior vesical plexus of veins. Cervical Bilharziasis may arise in a similar way.

So far as the local pathological changes are concerned the sclerotic form is described by some as the common clinical variety. This may be due to the fact that the early lesions are rarely seen because native patients do not readily submit to examination unless it is quite clear to them that they are suffering from some grave malady. Nevertheless the sandy appearance which is so commonly seen in the bladder has been observed on several occasions in the vaginal wall. Some authors have described the presence in Bilharziasis of numerous papillae arising

in the vaginal epithelium, and other observers have recorded the presence of Bilharzial ulcers. When the latter occur on the anterior wall they are generally connected with vesical or urethral Bilharziasis. Sinuses and fistulous tracks connecting the vagina with the bladder or urethra or both may be present. Girges has observed ulceration, infiltration, rugosities and papillomata in the vagina.

6 *The vulva*

Bilharzial disease of the vulva generally exists in the form of papillomatous masses which closely resemble the confluent type of condylomata lata of syphilis. Ulceration is present in some cases. It tends particularly to affect the vestibule, the hymen and, in some cases, the clitoris. The clitoris may cease to exist as the result of an extensive ulcerative process of this kind, in a similar manner the external urinary meatus may be destroyed. Papillomata from the base of the bladder have been known to protrude through the external meatus.

When the ulceration is accompanied by condyloma-like masses it is easy to mistake the condition for epithelioma of the vulva, indeed in some cases the two conditions co-exist.

In the cases which the writer has seen the papillomatous Bilharzial condition was found to spread as far laterally as the genito-crural folds, as far backwards as the anus and surrounding the anus and as far forwards as the highest point of the symphysis pubis. The diagnosis in the native is further complicated by the fact that so many of them have a positive Wassermann reaction, but the diagnosis is clear when plentiful ova are found in a scraping or on section or maceration of a piece of tissue removed at biopsy. Positive results are most likely to be obtained by the digestion method already

mentioned, indeed it is the method of choice

CASE RECORD OF VULVAL BILHARZIASIS

The patient was a young native female (No 3111) whose age was estimated as 8 years. She was brought to hospital by the mother, who complained that a mass of increasing size was present on the left side of the vulva. It had been noticed as a small nodule about 9 months before admission. On inspection a flat elevated irregular area was seen on the posterior half of the left labium majus and there were two elevated condyloma-like masses each about the size of a small pea, on the anterior portion of the same labium. The affected areas were excised and sent to the pathologist and the tissues exposed by the excision were treated by the actual cautery.

Pathologist's report

Morbid anatomy The dermal layer is greatly thickened and the underlying tissue is cellular in character. Minute points of calcification are noted. The macroscopic features are consistent with the diagnosis of condyloma.

Histology The main feature of the epithelium is the warty or condylomatous nature of the growth. There are one or two areas indicating early cell nest formation. In addition the deeper layers show a well-marked Bilharzial inflammatory reaction associated with Bilharzial eggs and tubercles.

Diagnosis Bilharzial condyloma of the vulva.

In this patient the Wassermann reaction of the blood was negative. Gonococci were not present in a smear but the ova of *S. haematobium* were plentiful in the stool. Only one specimen of urine was examined; ova were not found in it.

The child was given a course of antimony treatment.

It will be readily understood that conditions such as this, arising in young children, often progress until the whole vulva and surrounding tissues are affected. On the whole natives pay little attention to deviations from the normal, and it is not until the condition is advanced that they seek treatment. It may be taken that cases of extensive Bilharzial vulvitis have been present for many years. With the passage of time the ova

disappear or become so reduced in numbers as a result of the process of extrusion that they may be very difficult to find on routine histological examination. In the case of the young native girl recorded above Bilharzial ova were numerous. It follows that in old lesions the best procedure is to digest the tissue when the chance of finding eggs is much greater.

7 *The perineum*

The perineum may be the seat of Bilharziasis. When seen it is generally in an advanced state of ulceration and numerous sinuses may be present. Although perineal Bilharziasis may be associated with a similar infection of the anal canal, vagina or urethra, it sometimes occurs in the absence of any clinical signs of involvement of these organs. In such cases it is generally believed that it arises from the deposit of ova in the subcutaneous tissues. The chronic inflammatory areas gradually increase in size, finally breaking through the skin. They become secondarily infected very readily and ulcers and sinuses discharging offensive pus are produced. The curettings obtained from such tracks yield plentiful ova. In these cases there is generally extensive formation of extremely hard fibrous tissue.

8 *The broad ligaments*

It will have been appreciated from the description of Bilharziasis of the Fallopian tubes and ovaries that the broad ligament is a common site of the disease. The connective tissue elements between the two leaves of the broad ligaments are in direct continuity with the connective tissue planes and loose cellular tissue about the rectum and in relation to the bladder. The vessels of these structures pass through the connective tissue in

order to reach the viscera which they supply. One would therefore expect to find the earliest pathological changes in the connective tissue rather than in the viscera themselves. This is indeed exactly what takes place and it is the true underlying cause of most of the morbid manifestations of the disease. The broad ligament at its base is in close relation to the inferior vesical plexus of veins and through its upper and outer edges, the infundibulo-pelvic ligament, the ovarian vessels gain entry and exit. In the cases of genital Bilharziasis which the writer has observed, these structures were greatly enlarged and in more advanced cases they have been the seat of such fibrosis that the tissues cut with difficulty and produce a peculiar gritty sound as they are cut by the knife.

Now the organism which affects the urinary tract is *S. haematobium* and it follows that one might expect it to be the organism of cervical and vaginal schistosomiasis and perhaps even of the higher parts of the genital tract. From our knowledge of the venous system of this part of the body it is clear that the adult worms traverse the iliac veins and are to be found in these and in the inferior vena cava. The ovarian veins normally form a plexus between the layers of the broad ligament near the ovary and Fallopian tube and communicate with the uterine plexus. Two veins issue from the plexus and ascend in front of the external iliac artery, one lying on each side of the ovarian artery. The veins generally unite to form a single vessel which opens on the right side into the inferior vena cava and on the left side into the left renal vein. Presumably the adult worms are to be found in these structures as high as the renal veins. One might reasonably assume that when Bilharziasis of the genital tract is present there is also urinary Bilharziasis

affecting urinary structures from the kidneys downwards. The valves in these veins would not appear to be efficient barriers against the passage of adult worms or ova.

In all the cases of genital Bilharziasis which the writer has observed the organism has proved to be *S. haematobium*.

From the surgical point of view it will be appreciated that Bilharzial inflammatory tissue renders pelvic surgery very difficult. Great difficulty is experienced in separating the various organs and much skill and patience is necessary for the successful completion of operations undertaken for the relief of symptoms due to genital Bilharziasis.

The peculiarities of the disease as it is encountered in the genital tract rest primarily in the colossal fibrosis which is present and the absence of material resembling the caseous matter of tuberculosis.

In the cases of genital schistosomiasis which have been observed and investigated pathologically, *S. Mansoni* has not been found on one occasion. In Gelfand's case of tubal disease no mention was made of the nature of the ova found in the Fallopian tube and the fact that *S. Mansoni* were found in the stools means nothing as the two diseases frequently co-exist.

Gurges mentions that the broad ligaments sometimes contain fibrous masses 3 or 4 cm in diameter, they may be adherent to the ovaries.

THE CLINICAL ASPECT OF GENITAL BILHARZIASIS

Although in this paper it has not been possible to collect material relating to the effects of Bilharziasis on all aspects of gynaecology it is, however, possible to

record the common symptoms which may be associated with its presence

Puberty and the menopause

It will be clear to the reader that Bilharzial infection generally takes place early in life and for this reason it is important to determine the effect of the disease on the onset of puberty. Some writers have stated that the menses start late in infected girls. Girges states that menstruation may be delayed up to as late as 22 years. In others in whom the periods may have been established at or about the normal age, intervals of amenorrhoea amounting to 3, 4, 6 or more months may occur. These phenomena would suggest the early involvement of the ovary. With regard to the other end of reproductive life the menopause is said to set in early, even as early as 30 years of age. While this has not been my experience since most of the patients who have been under my care have had menses within the limits of normality it is nevertheless true to say that in many of the cases examined on the operating table the ovaries have been so extensively involved that it is reasonable to assume that if they had been left *in situ* they would have lost their function in due course. In view of the severity of the local change it is surprising that the menses have been so normal, one would rather have suspected that a condition resembling 'metropathia haemorrhagica' would have arisen as a result of persistent enlarged follicles. Further observations may prove that excessive and prolonged losses of the 'metropathic' type are more common than we have reason to believe at present. It would appear that in those cases in which puberty is delayed or the menopause extraordinarily early there must be considerable ovarian involvement, but the literature reveals a lack of direct observation in such cases.

Menstrual loss

Girges indicates that the menstrual loss may be scanty and its duration shorter than normal. This has not been found to be true of cases seen in this part of Africa. The explanation of scanty loss and short duration is not easy. It is, however, possible to associate it with extreme local fibrosis and vascular change resulting in the production of small quantities of the ovarian hormone or, in those cases in which the production of ovarian hormones is normal, the vascular change prevents them entering the blood stream in normal amounts.

Dysmenorrhoea

Dysmenorrhoea is a relatively common symptom, but it is not as constant a feature as one would imagine. It is generally an indication of severe involvement of the Fallopian tubes and broad ligaments.

Dyspareunia

Dyspareunia is generally complained of in the presence of tubal, ovarian and broad ligament Bilharziasis.

Leucorrhoea

Leucorrhoea from many causes is common among the native and it is, therefore, not easy to determine its significance in genital Bilharziasis. In cases of tubal schistosomiasis in the young unmarried female, leucorrhoea is rare, in fact Gelfand has suggested that the absence of leucorrhoea in a woman with a pelvic inflammatory mass is highly suggestive of Bilharzial disease.

Pain

Pain is a common symptom in advanced Bilharziasis, but not so common in the earlier stages of the disease. The pain is usually suprapubic in distribution and is frequently accompanied by low backache. In some cases colicky pain is complained of. Sometimes the pain is of sudden onset.

and is localized to the right or left iliac fossa when the possibility of ectopic pregnancy should be borne in mind. In addition to these common sites of pain mention should be made of pain associated with vesical activity.

Micturition

Frequency of micturition is common. Haematuria may be present. It may be possible to detect ova in the urine. In some cases a vesico-vaginal fistula may be present.

Sterility

Sterility may result from mild tubal Bilharziasis as well as from severe tubal infection. In those cases in which tubal occlusion is not complete ectopic tubal pregnancy is likely to arise with its usual group of symptoms.

General symptoms

Most patients with schistosomiasis suffer from general malaise, anorexia, dyspepsia and other vague symptoms. In those who have been infected young there may be abnormalities of development and retarded growth.

If normal intra-uterine pregnancy should occur it is reliably reported that the foetus often dies *in utero*. This is of considerable interest when considered in conjunction with the possibility of congenital infection which has been mentioned above.

In addition to the symptoms which have been outlined those cases of infection of the lower genital tract may present local soreness and pruritus, resulting from the passage of infected fluids from sinuses and fistulae over the perineal and vulval areas.

GENERAL MORBID ANATOMY

The general pathological features of genital Bilharziasis will have been appre-

ciated from the foregoing sections of this paper and little more need be said on this subject except to correlate some of the findings.

The ovary is not a common site of primary Bilharziasis, rather is it secondarily involved by tubal and broad ligament disease which may result in it becoming enclosed in a dense mass of adhesions. This is probably the reason why in so many cases of upper genital Bilharziasis the meninges remain within normal limits. In some cases the ovary may contain hard fibrotic masses which are occasionally so large as to replace the ovary.

The general appearance of tubal Bilharziasis varies considerably. In some cases the Fallopian tubes are generally but slightly enlarged and thickened and may present on the peritoneal surfaces a few small tubercles such as those commonly seen on the appendix in appendicular Bilharziasis. It is in those cases in which the Fallopian tubes show slight thickening that ectopic implantation of the fertilized ovum is likely to be found. In the more advanced cases and, incidentally the common type of case, the Fallopian tubes become so thick that they may be an inch or more in diameter. The mesosalpinx is similarly thickened. The ovary is generally involved and the whole forms a large hard mass which is increased in size by intestinal and omental adhesions.

Myometrial and endometrial Bilharziasis are rare. An insufficient number of authentic cases has been described to make a description of the naked eye features of any value.

In the broad ligament extreme thickening and fibrosis are the characteristic features. Occasionally fairly well circumscribed masses containing ova may be found.

The cervix, vagina and vulva present all the features of Bilharziasis which have been

described in other organs, that is, ulceration, haemorrhage, fibrosis and papilloma formation. Vesico-vaginal fistulae are relatively common.

OUTLINE OF THE TREATMENT

Most cases of genital Bilharziasis in the female call for surgical treatment of some variety. The Fallopian tubes and ovaries may need to be removed and in some cases of diffuse pelvic Bilharziasis the uterus may also have to be removed. Papillomata may be removed from the cervix, vagina or vulva and when the vulva is the seat of severe widespread disease a vulvectomy may be called for. Operative treatment of vesico-vaginal fistula in the presence of Bilharziasis always results in failure and in cases of this kind it may be necessary to resort to transplantation of the ureters.

- In all cases the urinary tract should be submitted to a thorough examination including cystoscopy and ureteric catheterization is often necessary.

The disease is treated with a preparation of antimony, preferably administered by the intravenous route. The initial dose for adults is $\frac{1}{2}$ grain, and the dose is gradually increased to a maximum of 2 to $2\frac{1}{2}$ grains. Injections are usually given on alternate days until a total amount of 25 to 30 grains have been given. It should be remembered that although the worms and the ova may be killed by antimony, symptoms may continue to exist and even become worse owing to the massive fibrosis which no amount of treatment with antimony will remove.

SUMMARY

An account is given of the history of Bilharziasis, the various types of schistosome which infest the human host and the

types of lesion which these parasites produce in human tissues.

The lesions of the urinary tract are described in so far as they affect or have any bearing on the genital tract.

The nature of Bilharzial disease of the female genital tract is dealt with organ by organ. In the cases seen by the writer the parasite has always been *S. haematobium* and nothing has been observed to date which indicates that *B. Mansonii* may be found in this region.

The most important clinical features are discussed and a brief outline of the treatment is given.

In the pathological investigation of specimens the importance of digestion of the tissue is stressed. It is considered to be more accurate than the ordinary histological procedure of section. In the case of Bilharzial lesions of considerable standing the ova frequently disappears leaving masses of chronic inflammatory tissue which give little evidence of the underlying cause. It is therefore contended that digestion of the tissues removed at operation is an essential part of the investigation.

S. haematobium is the organism which causes genital Bilharziasis in the female.

ACKNOWLEDGMENTS

This paper is based upon clinical material from the General Hospital, Salisbury, and my special thanks are due to Col. A. P. Martin, O.B.E., M.D., Director of Medical Services, for his kind permission to publish. My special thanks are also due to Dr. M. Gelfand, Government Pathologist, whose wide knowledge of Bilharziasis has proved very useful in the preparation of this paper and whose interest has been most stimulating. I also wish to thank the laboratory staff who have carried out the technical work.

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Premature Rupture of Membranes Effect On Labour At or Near Term

A REVIEW OF 320 CASES AND RESULTS

BY

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THIS paper discusses 320 cases of premature rupture of membranes occurring in a consecutive series of 2149 deliveries conducted at a wartime emergency maternity hospital in the years 1940 to 1942. The requisite data have been kept from the beginning of our work here, with this end in view, by means of special labour records. The keeping of these records and a steady policy of evaluating clinical findings has been greatly facilitated by the expert services of our senior nursing staff, who have remained unchanged during the 3 years of this study.

Chemical tests to confirm leakage of liquor amni were not made and the findings depend on clinical observations and on vaginal examinations made at the earliest useful opportunity. A small number of doubtful cases has been eliminated.

THE MATERIAL

A few observations on the nature of the material should be made. This hospital, opened in November 1939, has not functioned purely as a home for evacuee or refugee mothers where one might expect a normal sample of the Tyne-side community maternity work. For months there was no demand, or need, for our services and the hospital remained almost empty. It became necessary to attract abnormal midwifery and to offer

asylum to unusual and difficult cases from Tyneside and Northumbria outside the strict evacuation area, offering particularly our services to doctors and clinics who had pregnancy toxæmia cases on their hands in these areas. From the second half of 1940 the hospital has worked almost to capacity, and in 1942 the patients accepted have tended much more to be "normals," seeking their confinements in the peace of the countryside well away from the target areas of Tyneside. The 1942 cases, though much more of a normal series, consist mainly of primigravida women in the proportion of 61.4 per cent. This hospital also admits patients requiring special supervision and Caesarean section from Stagshaw House Maternity Home, in which some 600 confinements have been conducted in the war period. These selected admissions have raised the major operative obstetric rate somewhat above the usual maternity home standards. The material, then, is something between that of a maternity home, and that of a maternity hospital with a very high primigravida rate.

DEFINITION

Premature rupture of membranes is defined as having taken place when the rupture of the membranes precedes labour pains, recognized and acknowledged by the patient.

In approximately a quarter of the cases the patient was awakened in bed at night by a flooding of liquor amni and recognized within the hour that she was in labour. Such cases are included in my definition of premature rupture of membranes.

Precipitate labours or labour lasting less than one hour have been excluded.

GENERAL RESULTS

King,¹ in his key-paper on this subject, tabulates 34 series of cases of premature

TABLE I

No	Author	Year	No of cases	Length of labour	Inter-vention	Mor-bidity	Foetal danger
1	Dorman and Lyon	1921	270	Shorter	—	More	More
2	Polak, J O	1923	—	—	—	—	—
3	Brodhead, G L	1924	182	Shorter	Same	Same	Same
4	Randall, L M	1925	88	Same	—	—	—
5	Schulze	1929	604	Shorter	More	More	Less
6	Norris	1930	196	Shorter	More	More	Less
7	La Haye	1930	1274	Shorter	Less	Less	Less
8	Kreis	1931	1250	Shorter	Less	Same	Same
9	Fitzgibbon G	1931	220	Shorter	Same	Less	Same
10	Gutmacher and Douglas	1931	761	Shorter	Less	Less	Same
11	Slemmons, J M	1932	132	Shorter	—	Same	Same
12	Mason, L W	1933	166	Shorter	—	Less	Less
13	Morton D G	1933	150	Shorter	—	Same	Less
14	van Rooy, A H M J	1933	—	—	More	Less	—
15	Jackson	1934	500	Shorter	Less	—	Same
16	King	1934	300	Shorter	Less	Less	Same
17	King, E L	1934	—	Shorter	—	—	—
18	Woods	1934	750	Same	More	More	Same
19	Stern, S M	1934	85	Shorter	—	Less	Less
20	Holmes O M	1934	90	Shorter	Same	Same	Same
21	Rucker, M P	1935	716	Shorter	—	Less	Same
22	Krahulick E J	1935	205	Shorter	—	—	—
23	Williams	1935	100	Shorter	—	Same	Same
24	King	1936	597	Shorter	Less	Less	Same
25	Spademan L C	1936	—	Shorter	Same	Same	—
26	Ballard M B	1936	425	Shorter	Same	Same	—
27	Plass and Seibert	1936	681	Shorter	—	More	—
28	Essen-Mueller	1936	1000	Shorter	More	Same	Same
29	Mathieu and Holman	1937	750	Shorter	—	More	Less
30	Sunde	1937	1280	Shorter	—	More	Same
31	Wichman	1937	360	Shorter	Same	Same	Same
32	Tennent R A	1938	357	Shorter	—	—	—
33	Wetterdal	1938	1022	Shorter	—	—	Same
34	Hauch E	1938	220	Shorter	—	Same	—
35	Morton <i>et al</i>	1942	1000	Shorter	More	Less	Less
36	Greig D S	1942	310	if near term Same	Same	More	Less

rupture of membranes studied between 1921 and 1940. The results are remarkably unanimous that labour is shorter, while in general the total evidence indicates that intervention, morbidity and foetal loss are not markedly, if at all, increased. This table is here printed (Table I) to which I have added as numbers 35 and 36 the recent figures of Morton *et al*² and my own.

It should be noted from Morton's very careful analysis that if he omitted all cases of less than 38 weeks gestation, all his figures, except that of "intervention," would appear to show that premature rupture of membranes was a most favourable factor.

Table II is given to show the results of 320 cases of premature rupture of membranes in straight contrast with the general hospital statistics.

and propose to discuss results with two fairly comparable series of cases—one with premature rupture of membranes, the other an orthodox series—using the remainder

CASES ELIMINATED

- 1 Elective Caesarean section
- 2 Prematurity below 36 weeks
- 3 Accidental antepartum haemorrhage
- 4 Placenta praevia
- 5 Admitted for relief of dead foetus (membranes intact).
- 6 Surgical inductions
- 7 Foetal deformities
- 8 Born before arrival
- 9 Precipitate labour, or labour apparently lasting less than 1 hour

This selection eliminates 159 cases, leaving for comparison

TABLE II

	No of cases	Stillbirth	Neonatal deaths	Morbidity	Caesarean section	Intervention	Maternal deaths
Premature rupture of membranes	320	3 (1.0)*	4 (1.3)	5 (1.6)	5 (1.6)	19 (6.0)	Nil
Total	2149	51 (2.4)	49 (2.3)	28 (1.3)	63 (2.9)	148 (6.8)	5

* Figures in parentheses denote percentages

Any synopsis of results such as is given in Table II must, almost inevitably, show premature rupture of membranes in a favourable light since the total hospital figures are loaded with the whole incidence of abnormalities such as prematurity, haemorrhagic emergencies, severe toxæmias requiring induction of labour, admissions for dead foetus and the like. A fairer comparison can be made by taking an unhandicapped series of labours wherein the infants involved are similar in term of gestation and uncompromised by highly abnormal conditions such as antepartum haemorrhage, surgical inductions and foetal deformities. Accordingly I have eliminated the following classes of cases

(a) A series of 310 cases of premature rupture of the membranes

(b) A series of 1680 cases of orthodox labour

Both series, then, comprise all our labours at or over 36 weeks gestation when the onset was not compromised by haemorrhage, previous foetal death or severe foetal abnormality but including all cases of disproportion, malpresentation and the usual hazards of midwifery.

Incidence

The incidence of premature rupture of membranes may be noted in passing since it is a figure rarely given. In this series it is 18 per cent.

Parity

Of 310 cases of premature rupture of membranes 196 occurred in primigravidae and 114 in multiparae. The primigravid rate is therefore 63 per cent. The total hospital primigravid rate is 57 per cent. The incidence of premature rupture of membranes would thus seem not to be greatly affected by the parity.

INFLUENCE OF TOXAEMIA

Of 310 cases of premature rupture of membranes 35 were toxæmic, an incidence of 11 per cent. This compares with an all over toxæmia rate of 12 per cent for the total of 2,149 cases, and 10 per cent for the selected 1,690 cases. Apparently the influence of toxæmia on premature rupture of membranes is negligible.

(Note—For the purposes of our records a case to be rated as suffering from hypertensive toxæmia must show any two of the following three criteria

- (a) Blood-pressure rate over 140/90
- (b) Albuminuria, confirmed if slight by catheter specimen
- (c) Oedema (other than transient oedema of the feet)

INFLUENCE OF PRESENTATION

In 310 cases of premature rupture of membranes, the presentations were

1st vertex	155
2nd vertex	96
3rd vertex	29
4th vertex	10
Twins	8
Breech	11
Transverse	1
	<hr/>
	300

In the total selected series of cases being considered, i.e., in 1,990 cases there were 150 occipito-posterior positions, 45 breech

cases and 21 twin pregnancies. These patients suffered premature rupture of membranes in the following percentages

- (a) Occipito-posterior 39 in 150 = 26 per cent
- (b) Breech cases 11 in 45 = 25 per cent
- (c) Twin pregnancies 8 in 21 = 38 per cent

All three figures are well above the general percentage suffering premature rupture of membranes, viz. 18 per cent. These figures confirm both clinical impression and orthodox teaching that the abnormal presentation is often associated with premature rupture of membranes, but oddly enough in this series are found 2 brow, 4 face and 6 transverse presentations—12 highly abnormal presentations—only 1 of which sustained premature rupture of membranes.

Twelve cases of prolapse of the umbilical cord occurred in the total series of 2,149 cases. Not one was associated with premature rupture of membranes.

ONSET OF LABOUR

In the majority of cases labour has a recognizable clinical onset within 1 hour of the rupture of membranes. In a minority there is delay, usually for some hours, rarely for some days, and occasional reports of long periods are made.

The former class of case might well be called initial rupture of membranes, the latter true premature rupture of membranes. Table III gives the proportion of our cases in respect of this distinction with further subdivision into primigravidae and multiparae.

Immediate onset of labour occurred, therefore, almost exactly in 60 per cent of the two series of primigravidae and multiparae.

The delay in onset of labour in Class A, i.e., in primigravidae, varied from 2 hours to 120 hours, with an average period of 17½ hours.

TABLE III

Class A = Primigravidae cases with delay in onset of labour >1 hour	79
Class B = Primigravidae cases with no delay in onset of labour	117
Class C = Multiparae cases with delay in onset of labour >1 hour	48
Class D = Multiparae cases with no delay in onset of labour	66

The delay in onset of labour in Class C, i.e. in multiparae, varied from $1\frac{1}{2}$ to 73 hours, with an average period of 17 hours

It would be tedious to give all the tables which I have worked out for the various sequelae and abnormalities divided into those classes A, B, C, and D, and the figures become so small as to be practically worthless, but it may fairly be noted that only 2 of the 5 cases of morbidity were in the "delay in onset of labour" groups, while out of 7 cases of stillbirth and neonatal death as many as 6 occurred in the groups with no delay in onset of labour. There was no significant variation in operative and intervention rates in the two groups

DURATION OF LABOUR

Table IV gives the duration of labour, 1st and 2nd stage, and totals for all four classes of cases and the corresponding figures for primigravidae and multiparae in the selected series of 1,680 orthodox labours

The duration of labour in my series, then, is identical for primigravidae and slightly shorter for multiparae with premature rupture of membranes. The difference is so trivial that I have answered the "Length of Labour" column in No. 36 of Table I as "Same"

It is noted that labour is appreciably shorter in patients in whom rupture of membranes is not attended by delay in onset

In 59 cases of premature rupture of membranes the patients came into labour at the 36th, 37th, and 38th weeks. The duration of labour has been worked out for these in Table V

The subtraction of this premature series does not markedly affect the figures given in Table IV and the conclusion made that "Length of Labour" is "Same" can stand

CAESAREAN SECTIONS

Five Caesarean sections became necessary in the course of labour in the series of 310 cases of premature rupture of mem-

TABLE IV

	No.	1st stage (hours)	2nd stage (hours)	Total hours	
Class A	79	17½	1¼	18¾	Primigravidae
Class B	117	15	1¼	16¼	
Class C	48	8½	½	9	Multiparae
Class D	66	7	½	7½	
Orthodox Labours (1680)					
Primigravidae	996	16	1½	17½	
Multiparae	684	9¼	½	9¾	

TABLE V DURATION OF LABOUR AT 36TH 37TH AND 38TH WEEKS

	No	1st stage (hours)	2nd stage (hours)	Total hours
Class A	13	14	1	15
Class B	27	16	$1\frac{1}{16}$	17
Class C	12	10	7	10 $\frac{1}{2}$
Class D	7	5	$1\frac{1}{2}$	5 $\frac{1}{2}$

branes, a rate of 1.6 per cent. The indications were

Transverse lie in a virtual primigravida 1
 Prolonged labour for cephalopelvic disproportion making poor progress 3
 Dystocia dystrophica syndrome 1

Except in the case of transverse lie, the operations were by lower segment Caesarean section under spinal anaesthesia, the membranes having been ruptured for 6, 24, 31, 33 and 46 hours. All the patients made fair recoveries, one being morbid by Ministry of Health standards, but not seriously ill. Her membranes had been ruptured for 33 hours. All the babies were secured alive and did well.

The Caesarean section-rate for the whole hospital series plus cases admitted from Stagshaw House is approximately 2.4 per cent. The rate for the 1,680 selected labours was 1.5 per cent, approximately the same as the figure for the premature rupture of membranes series.

FORCEPS

Forceps extraction was employed in 19 of the 310 cases, a rate of 6 per cent, of which 18 were primiparae (total 196), giving a primiparous forceps-rate of 9.2 per cent. This figure is low by any standard and is to be contrasted with our total hospital forceps-rate in primiparae of 9.8 per cent.

OTHER INTERVENTIONS

Two other primiparous patients had cervical incisions and application of traction

by Willet's forceps for dystocia dystrophica syndrome after 73 and 35 hours labour respectively. Both patients made non-morbid recoveries and both babies were secured alive and did well.

The intervention-rate in the series can be returned as "Same" in No. 36, Table I King's "Intervention" column.

MORBIDITY

The general morbidity-rates have already been shown in Table II. It remains to contrast the morbidity-rates of the 310 cases of premature rupture of membranes with the rate of 1,680 orthodox cases. The standard employed is that of the Ministry of Health as used for notification of puerperal pyrexia. The rates are

Premature rupture of membranes 310 cases
 5 morbid (1.6 per cent)
 Orthodox labour 1680 cases 21 morbid (1.25 per cent)

Of the 5 morbid cases in the premature rupture of membranes series, the causes given are

Uterine infection 2 (1 being by haemolytic streptococci group A)
 Transfusion reaction 2 (nil found on bacteriological examination)
 Breast abscess 1

For the better assessment of results I have kept a secondary morbidity-rate in our hospital, using the wording of the Ministry of Health Regulations, but substituting 99.4 for the figure 100.4. The

various morbidity-rates using this standard are

All cases	2149	86 cases = 4.0 per cent
Orthodox Labour	1680	61 cases = 3.6 per cent
Premature rupture of membranes	310	13 cases = 4.2 per cent

It would seem, therefore, that using both standards of morbidity, the premature rupture of membranes series is slightly unfavourable, and the answer in the morbidity column of Table I must be "More"

PROLONGED LABOUR

For the purposes of this study, any labour lasting longer than 30 hours is deemed prolonged

In the total of 2,149 cases we have had 160 such cases. In the selected series of 1,990 labours there have occurred 150 prolonged labours, and it is these which are discussed here

TABLE VI

INCIDENCE OF PROLONGED LABOUR

Orthodox labours	1680	119 cases = 7.0 per cent
Premature rupture of membranes	310	31 cases = 10.0 per cent

or, on considering primigravid labours only

Orthodox labours (primip)	996	112 cases = 11.3 per cent
Premature rupture of membranes - (primip)	196	29 cases = 15.0 per cent

It would appear that the chances of pro-

longed labour after premature rupture of membranes are sharply increased, and that nearly 1 primipara in 6 will have the traditional long, dry, labour, or in other words, that a primipara who sustains premature rupture of membranes, is 50 per cent more likely to have delayed labour in some form

Table VII shows the distribution of the cases of delayed labour among the Classes A, B, C and D, given in Table IV

It would appear that delayed labour is more liable to occur when there is delay in the onset of labour after the accident of premature rupture of membranes

FOETAL RESULTS

Foetal results are shown for the two contrasted series

	Premature rupture of membranes (310 cases)	Orthodox labours (1680 cases)
Neonatal death	4 = 1.3 per cent	24 = 1.4 per cent
Stillbirth	3 = 1.0 per cent	24 = 1.4 per cent
Total	7 = 2.3 per cent	48 = 2.8 per cent

The foetal loss is, then, somewhat lower in this particular series of cases and this corresponds with most findings of the various observers quoted in Table I. The total number of losses (7) is so small that deduction becomes untrustworthy and small accidents having little relation to the normal hazards of midwifery can change the percentages in a misleading manner. The briefest possible clinical notes of the 7 lost babies is appended

TABLE VII

	No	Delayed labour over 30 hours	Percentage	
Class A	79	14	18 per cent	} Primigravidae
Class B	117	15	13 per cent	
Class C	48	2	4 per cent	} Multiparae
Class D	66	0	-	

Stillbirths

1 Case 169 Primiparous breech Sluggish uterine action for 40 hours in 1st stage Baby lost by parietal fracture in assisted delivery—should have had Caesarean section

2 Case 338 Hypertensive toxæmia Intrapartum death half way through long 1st stage lasting 70 hours

3 Case 888 Sudden foetal death near end of satisfactory 1st stage lasting 31 hours No external haemorrhage but large retroplacental clot of recent origin found on delivery 2 hours later No evidence of toxæmia Abruptio placentæ

Neonatal deaths

1 Case 88 A second atelectatic twin delivered by breech extraction for severe hæmorrhage between 1st and 2nd babies Died aged 24 hours

2 Case 450 Death of apparently normal infant on 4th day from severe melœna

3 Case 1020 Easy normal primiparous delivery Baby died at 16 hours with symptoms of cerebral hæmorrhage

4 Case 1452 First twin died of acute enteritis on 13th day Other twin normal

It can be seen that two neonatal death losses had no relation to the circumstance of premature rupture of membranes, or of labour and that the first stillbirth quoted was entirely due to faulty judgment

On the whole I am inclined to think that foetal loss after premature rupture of membranes is less and I have so entered this opinion in the final column of Table I A suggestion is made that loss is lessened by better care and fuller attention being paid to the foetal heart condition in a labour thought to be prejudiced at the outset

DISCUSSION

The title of King's key-paper¹ was "Newer Concepts of Dry Labour" King appears to feel that Denman² went too far when, after expounding his hydrostatic wedge theory of cervical dilatation, he deduced from this theory that rupture

of the membranes led to a "derangement of labour and tended to protract rather than shorten labour" Denman, says King, appears to have crystallized opinions for a century and with the whole German school giving its sanction, the teaching of (1) the need for water-bag dilatation, and (2) the concept of a slow dry labour have persisted in our textbooks to this day Kreis⁴ seems to have made the first scientific approach to the subject by rupturing the membranes deliberately early in the labour of 1,250 consecutive cases He found that (a) labour was shorter, (b) intervention was less, (c) morbidity was the same, and (d) that foetal loss was the same The mass of evidence compiled by King and given here in Table I mostly follows the same lines and justifies the title of King's paper A very interesting study, something along the same lines as this paper, was made by H Fredrikson who studied 1,290 primigravidae and 1,300 multiparae "who had normal occipito-anterior presentations in which babies weighed 2,500 grammes and over" He found premature rupture of membranes in 12 per cent of primigravidae and 10.7 per cent of multiparae and he gives as his findings (a) labour shortened (b) morbidity twice as often, and (c) foetal mortality not increased

Wetterdal⁶ pursued the matter still further in his study of 4,000 parturitions followed up 12 years later His conclusion was that the premature rupture of membranes affects neither the mortality, primary or late, nor the percentage of mentally and physically defective children

This mass of evidence is striking enough and unusually unanimous, but there must yet remain some doubt as to whether "dry labour" is so safe, easy and even advantageous It is unlikely that a theoretical deduction made by Denman 130 years ago has bemused not only our textbooks but has also raised a false bogey for

all practising obstetricians for several generations. The old concept of "dry labour" as one demanding, upon occasions, all the patience and skill of the attendant, often the full mental and physical resources of the patient, cannot have been entirely imaginary. While we may abandon Denman's mechanics of labour and while we may well agree that most cases of premature rupture of membranes will pass off smoothly, especially in a case near term with early onset of labour after the liquor amnii is lost, there still must remain a doubt in the minds of every clinician. This paper appears superficially to endorse the new concept of "dry labour." But here, upon further analysis, we find that the incidence of prolonged labour over 30 hours is sharply increased after premature rupture of membranes—that in the Class A Series, i.e., primigravidae with delay in onset of labour after loss of liquor, this incidence is as high as 18 per cent, compared with 11 per cent for primigravidae with normal onset of labour. The prolonged labours varied greatly in quality showing all grades of inertia from the slow, feeble, irregular, sluggish uterus, through various degrees of colicky uterus to the full-blown dystocia dystrophica syndrome. I mention, as a matter of clinical observation, that I was generally unable to prognose a delayed labour from the state of ripeness of the cervix at the time of rupture of the membranes.

An increased incidence of prolonged labours need not necessarily give bad results. That may be the true inference to be drawn from the 36 successful series of cases reported in Table I. In my own series, the labour record is prominently marked when a case of premature rupture of membranes is diagnosed. This leads to an increased watchfulness over the foetal heart and a considerable amount of nasal oxygen

has been administered to the mothers in both stages of labour, particularly if irregularity has been noted, or as a preparation for interference. General anaesthesia is avoided whenever possible, spinal or local pudendal anaesthesia being substituted. On the whole the tendency is to carry conservatism rather further than for the normal cases. After the first year, covering about the first 100 cases, I abandoned the use of vaginal instillations when membranes were ruptured over 24 hours and did not find any disadvantage.

Professor Young has pointed out that good results, especially freedom from morbidity and intrapartum infection, may be due to good environment. This point is accepted. Our unit, with its low morbidity-rate and an adequate number of separate labour wards, managed by a staff living healthily in the country, gives adequate environment for these troublesome cases. A similar series of cases treated in less "clean" surroundings might well produce the bad results of maternal sepsis and foetal loss which were part of the old concept of "dry labour."

CONCLUSIONS

- 1 Three hundred and ten cases of premature rupture of membranes are considered in contrast with a series of 1,680 cases having an orthodox onset of labour.

- 2 Prematurity has been excluded. Only cases over 36 weeks gestation are considered.

- 3 There is a definite increase in the incidence of premature rupture of membranes in cases of abnormal presentations such as occipito-posterior, breech and twin presentations.

- 4 Parity and toxæmia are not factors in producing premature rupture of membranes.

- 5 On average, over a series, the length of labour is not increased.

6 In 60 per cent of cases, the premature rupture of membranes and the onset of labour are clinically simultaneous. Labour is appreciably shorter than normal in this class of case.

7 When there is delay in the onset of labour after loss of liquor amnii, labour is appreciably longer and there is a noteworthy increase in the incidence of prolonged labour over 30 hours. Here, probably, is the justification for the old concept of "dry labour."

8 Intervention can be kept at least to normal limits in cases of premature rupture of membranes.

9 Good results can be obtained by careful management. These results should be as good as for a normal series of cases. Good environment is a prerequisite.

I have to thank Dr John B. Tulley, Medical Officer for the County of Northumberland, for his courtesy in giving me permission to use the records of Dilston Hall Maternity Hospital in preparing this paper.

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Vesicovaginal Fistula

A REVIEW OF 65 LOCALLY INOPERABLE CASES TREATED BY
TRANSPLANTATION OF BOTH URETERS INTO THE PELVIC COLON

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THE patient who is a sufferer from a vesico-vaginal fistula has indeed a miserable life, a fact which has been known since the very earliest of times, for in ancient literature the condition has been described as a curse, and in more recent books as the greatest social disease it is possible to conceive.

No truer statement than this could be made as it is difficult to imagine a more dreadful condition than that of being constantly wet and continuously drawing attention to the affliction through the olfactory organs of those with whom the patient comes in contact.

A vesicovaginal fistula may be caused by injury such as a wound through the vagina and/or abdominal wall involving the bladder, or by fractures of the pelvis. This type of fistula usually heals up in a short space of time, because the blood supply to the part is intact and there is no tissue necrosis. The term vesicovaginal fistula, however, as described in gynaecological books, envisages that intractable type caused by difficult labour. Here the lesion is the result of delay in the progress of the child through the birth canal, with the result that pressure is brought to bear by the child's head on a part of the bladder wall, so that there is stoppage or interference with the blood supply, resulting in tissue necrosis and sloughing of the

affected portion of the bladder. Such a fistula may also be caused by injury at an operation, or in association with carcinoma. The aetiology will not be further dealt with, as the object of this paper is to discuss the treatment.

Occasionally, and if there is some blood supply intact, such fistulae will heal up of themselves in the first few weeks after they are first noticed. However, if this happy and unfortunately rare event does not take place within 6 weeks then one must have recourse to operative interference, a review of which may not be out of place at this stage.

Before Marion Sims made his great discoveries nearly a century ago, whereby he was enabled to see fistulae and partially get over the difficulty of un-absorbable sutures, these cases were all deemed hopeless and nothing could be done for them except the simplest of palliative treatment devised to sop up the urine, and obviate the smell. Though Sim's use of his speculum and of silver wire was the first great step in the successful treatment of vesicovaginal fistulae, yet he was not as successful as he hoped, owing to the lack of true aseptic methods. The keynote of his operation was the edge paring of the fistula opening and though it is usual to-day to dissect out flaps, edge paring is by no means

obsolete Nowadays, when the operator can see the fistula, and indeed it is essential that he should be able to get a good view of his operative field, the operation is chiefly that of dissection and separation of the vaginal wall from the bladder wall, and the suturing of each of these separately without any tension. However, in order to obtain a good result, the patient must first have been examined for constitutional and/or specific disease, and these eliminated. The fistula must be of moderate size, for one which is of pin-point size, or one which is bigger than a shilling, will not be repairable by this method. The fistula must not be adherent to other pelvic structures, specially the bony pelvis. For the treatment of these large fistulae, specially those lying posteriorly, the new operation of McAlpine may be carried out with success, but on the whole we favour the operation of transplantation of the ureters into the pelvic colon in cases of fistulae deemed inoperable by the usual method via the vaginal route. We have not had actual experience of McAlpine's operation, but in the Eden hospital we have carried out ureteric transplantation in a number of cases with considerable success, and we are convinced from the results of our technique, that this operation is one which should be performed more often than it is. However, there are different points of view and a colleague of ours told one of us (H E M), that in his opinion transplantation of the ureters should seldom if ever be done, and he himself had not yet come across a vesicovaginal fistula which he was not able to repair locally. The reply was "Well some day you will."

A certain amount of difference of opinion regarding the operation itself has been recorded, and while some authorities agree with us that the two-stage operation is preferable, others, notably Henry Wade of Edinburgh, are definitely in favour of a

one-stage operation. The danger of the one-stage operation is the onset of anuria with fatal result. Wade states that this danger can be obviated by the early administration of sodium sulphate, but while we have no doubt that this eminent authority speaks as a result of his great experience, we feel that he has a different type of patient to deal with than we have in Calcutta, and from our experience of a very large number of cases of the condition of vesicovaginal fistulae which we see in this country, we state that the one-stage operation is here inadvisable. Our patients come from the extremely poor, ill-nourished class. They are ignorant and frightened, and have been through a truly dreadful time in labour without any efficient help, facility, or even in many cases sympathy. They have had a stormy puerperium. They have had no antenatal advice, and many of them have never seen a doctor before they come for treatment for the fistula. Most of them have for years been suffering from kala-azar, malaria, dysentery, helminthic disease, to mention but a few conditions, and may present evidence of privation and lack of vitamins. Also they have no idea of what is going to happen, as they have never been consulted in the matter, the husband having arranged all. Their resistance is therefore so low that they would be unable to stand the risk of the one-stage operation. We therefore have had little or no experience of anuria in our cases.

The second great danger, that of ascending septic infection from the bowel to the kidney pelvis has again happily been conspicuous by its almost complete absence, and this we are convinced is the result of careful choice of cases (all those suffering from specific or general diseases being excluded from operation), careful and full pre-operative treatment, and above all good nursing afterwards. In this latter respect we are fortunate in having in Staff-

nurse Lewis one of the most perfect and painstaking nurses in this country, and we here state categorically that our success is due in no small extent to her thoroughness in the post-operative treatment of our cases.

The condition is almost entirely confined to the class of patient mentioned above, and rarely does one see a case among the well-to-do, for they, like the general public in the United Kingdom, are year by year becoming more universally medically minded, and so are more and more ready to seek antenatal advice. Not the least interesting item in the history is the long duration of the condition before help is sought, and it is common to be told by the patient, or her husband, that the lesion has been present for many years, anything from 5 to 12 years being commonplace, and one quite recent case admitted to 17 years. In the United Kingdom, and America, in other parts of the world including the well-to-do population of this country, such a length of history would be quite impossible, but among such people as the peasantry of India where the woman has no say in the matter, she just has to await the decision of her husband and suffer in silence till the spirit moves him, and there may be many reasons for delay from his point of view, the chief of course being that he has not got the fistula.

The result of the operation is excellent, the patients being able to hold urine in the rectum for at least 2 hours, and some for as long as 4 hours, the average amount held being some 8 ounces. When it is remembered that a little fluid injected into the rectum immediately runs out again, one wonders how the rectum can educate itself to retain the urine as described. The fact remains that it can and does. Let us call to mind that sound surgical dictum "Structure adapts itself to function" and correlate how the adaptation takes place. What happens is that the patient is given

a cloaca and she becomes turned into an individual with, as it were, her unrogenital sinus apparatus non-separated from that of her bowel, so that she now has a urodaeum where the urine collects, separated from her proctodaeum.

OPERATION

The right ureter is chosen for transplantation first. The abdomen is opened by right paramedian incision. The uterus is lifted forward. Small and large intestines are pushed above and aside from the field of operation. The right ureter is identified.

The ureter crosses the brim of the pelvis just near the sacro-iliac junction, and makes peristaltic movements under the posterior peritoneum like a round worm (vermiculate). The peritoneum at the optimal site is picked up and incised with a sharp scissors. Sometimes the ureter is missed when it is adherent to the posterior peritoneum. The ureter is picked up and separated from surrounding tissues preserving very carefully the minute blood-vessels which run along its surface, for its vitality will suffer if it is stripped of its blood-supply. The pelvic part of the ureter is carefully traced behind the broad ligament up to the bladder, where it is clamped between two artery forceps, the vesical end being cauterized with carbolic acid and buried. The upper portion wrapped in a piece of gauze is for the time being placed out of the way on the anterior abdominal wall.

The upper part of the rectum which is selected for the implantation must be devoid of appendices epiploicae. An oblique incision is made on the antero-lateral wall of the rectum. The incision should be deepened as it proceeds downwards and all bleeding points are picked up with fine artery forceps and tied off. With a tenotomy knife a stab wound is made through the lumen of the rectum. The

ureter is now brought forward from its resting place on the abdomen, and its end is shaped into a wedge the portion that is cut away being taken from its posterior aspect. This wedge point is then transfixed and a long thread of catgut drawn through. There is a needle at each end of the thread, which is to avoid tearing out of the catgut as a result of the tension caused by subsequent threading. These two needles are then successively introduced into the lumen of the bowel, and brought out through its anterior wall at least half an inch from the lower end of the stab wound. Traction now brings the shaped end of the ureter into the bowel and the threads are tied. The ureter now lies on the ventral aspect of the rectum in the gutter made for it, where it is anchored by two sutures passing through the cut edges of the original incision and the anterior wall of the ureter. Its upper freed portion is then buried after the method of Weitzel, peritonized by Lambert sutures, and finally fixed to the mesentery. The cut margins of the posterior peritoneum are repaired. Thus the ureter now lies in the wall of the rectum before it enters the lumen of the bowel, which arrangement is similar to its course in the bladder wall (an effective valvular control over the exit of urine). The abdomen is closed in layers. The left ureter is similarly dealt with 4 weeks later.

SPECIAL POST-OPERATIVE TREATMENT

(a) The body fluid is maintained by continuous drip of saline and glucose, 5 per cent.

(b) A rubber tube is kept in the rectum for drainage of urine. Do not expect urine to be expelled from the rectum for 12 to 18 hours.

(c) If anuria or uraemia is threatened, administer intravenously sodium sulphate 0.48 per cent by the continuous drip method.

Within reason the longer the incision in the rectal wall is, the better, as the valvular opening is thus rendered more efficient, and consequently the potentiality of the onset of sepsis is lessened.

For the first few days the patient's condition is stormy. She is restless and irritable, so that great patience in nursing her is required, and it is in these critical first 5 or 6 days that the surgeon must have the services of a good nurse, for it is she who at this stage makes or mars the final result.

For 10 days, steady and continuous drainage through the tube must be maintained, and the rectal contents kept in a fluid state. The patient should be made perfectly comfortable (by hypnotics if necessary), and all fears allayed. During convalescence it is advisable for the patient to take magnesium sulphate or some other form of purgative salts in order to ensure that the faeces will be constantly in a semi-fluid condition.

A vesicovaginal fistula is a comparatively rare occurrence in the United Kingdom, and for this reason the literature on the subject is somewhat meagre. The modern textbooks but briefly touch on the lesion, and one seldom comes across it as the subject of a paper in the medical periodicals.

In a recent communication Gladys Dodds calls attention to the fact that 6 to 8 weeks after delivery is the optimal time to repair a vesicovaginal fistula by local operation. This, of course, is correct, but we have never seen such an early case due to obstetrics. She further states that spontaneous cure of fistulae even of 1 inch in diameter may take place, and that such cure is greatly assisted by the presence of an in-dwelling catheter.

We are carrying out this local treatment at present in a case of a vesicovaginal fistula following the operation of hysterectomy in our own hospital, but obstetri-

cal vesicovaginal fistula come to us so late that the lesion is in such a state of cicatrization and fibrosis, that any other treatment but surgery is contra-indicated

RECORD OF ANALYSIS

Below is the record of 65 cases in which both ureters were transplanted. In 61 of these cases the operation was two stages, in 5 one stage

Aetiology

- (a) Congenital, 2 cases
- (b) Traumatic (accidental), nil
- (c) During labour—
 - Normal pelvis
 - Confinement with instruments, 7 cases
 - Without instruments but prolonged labour, 11 cases
 - Contracted pelvis
 - Confinement with instruments, 13 cases
 - Without instruments but prolonged labour, 20 cases
- (d) As a result of operation (following operation for elephantiasis vulvae, performed in a district hospital), 1 case
- (e) Following radium therapy for carcinoma of cervix, nil
- (f) Due to carcinoma of cervix, bladder and vagina, nil
- (g) Cause not traceable, 11 cases

Result

Cured, 51 cases, 78.5 per cent

Death, 14 cases, 21.5 per cent

Out of 14 deaths, 3 occurred after transplantation of both ureters in a single sitting. Excluding these 3, there is a death-rate of only 11 in 61 cases, a percentage of 16.4.

A little comment is necessary on the high death-rate after the one-stage operation.

Indian patients generally display little resistance to a serious, and above all prolonged, operation, no matter what the anaesthetic may be. Our cases were given ether, chloroform, gas and oxygen, spinal

anaesthesia, according to choice and state of the patient. Out of 65, 49 had a fistula following difficult or delayed labour. The majority of patients, though young, suffer severely during the puerperium. They become easy victims of tropical fever or helminthic disease. Mental worry, inferiority complex, privation, general ill-health, climatic condition and malnutrition, all play their parts and take their toll.

In our series 33 were multiparae, of which 11 had history of repeated stillbirths. In 8, local repair (vaginally), was attempted, but in 2 cases there were recurrences (following childbirth) which proved irreparable. In 6 cases local repair failed in spite of the utmost care, and in these operative interference was deemed inadvisable.

It would be very interesting to follow-up such cases, but unfortunately very few return, from such reasons as financial difficulty, want of opportunity, ignorance of the value of doctor's advice, and the difficulty of making them understand why they should return. We know, however, that if unsuccessful, or more treatment is required, the Eden Hospital patients always come back to us, so we flatter ourselves that as these patients seldom return, our operation has been a success.

One patient, during the first operation, was found to be 2 months pregnant, which, however, made no difference to her successful convalescence at both operations. Her pregnancy continued and she had her baby by Caesarean section at term. (A case of contracted pelvis).

Another patient who had had both ureters transplanted 18 months before, came into hospital at term for confinement. Caesarean section was ordered for the following day, but the patient suddenly came into labour that evening and after 4 hours gave birth to a baby, 5 pounds 12 ounces, without the slightest trouble or injury to the site of implantation.

Breech Presentation in the Elderly Primipara

BY

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FOR a considerable time it has been known that the foetal mortality in breech presentation has been unsatisfactory, but I do not think it has been sufficiently recognized how lamentable is the position with regard to the elderly primipara

In the Manchester school we have been aware of this to a certain extent as shown by the high percentage of Caesarean sections performed in this type of case as compared with other clinics, but it has only been by investigating the cases over the last decade that it has become clear how appalling the foetal mortality has been by vaginal delivery

It has been difficult to assess definitely the foetal mortality in breech deliveries in general, owing to the very varied standards of correction which are used by different hospitals and authors. The type of cases which are excluded from the corrected mortality vary enormously, as pointed out by Gibberd at the 1931 meeting of the British Medical Association. "The official way of presenting breech mortality figures has the effect of hiding to a great extent the seriousness of this type of labour." The position is even more confused in the case of the elderly primipara, and in this paper I have used 30 years of age as the lower limit, as the relatively few articles on this subject give only a small series of cases. In spite of this, however, and the fact that owing to service duties I have not been able to review the literature or hospital reports as adequately as I would have liked, a reasonably accurate impression can be gained

Gibberd¹ from a study of the figures of a number of English maternity hospitals, gave the following figures. In uncomplicated cases (corrected mortality) foetal deaths, 26 per cent, neonatal deaths, 6 per cent. This is for all cases, and I think it only right to assume, as will be shown later, that these figures would be much higher in the elderly primiparae group. In the same paper he states that the uncomplicated foetal mortality in primiparae of all ages at Guy's Hospital over a period was 28 per cent. Gairdner, Jackson, and Jackson,² give the following short series: uncomplicated breech cases in private practice, 27 vaginal deliveries with 8 deaths, in hospital, 36 vaginal deliveries with 9 deaths, by Caesarean section, 26 breech cases with 1 foetal death which can be excluded from the corrected figures as it was a monstrosity with hydrocephalus.

The following figures refer, in every case, to breech presentation. Patton and Mussey,³ out of 131 primiparae of all ages, delivered vaginally, had a foetal mortality of 21.37 per cent. They state that their corrected foetal mortality was 5.34 per cent, but they do not give their standards of correction. Their corrected foetal mortality in multiparae was 2.23 per cent. Six Caesarean sections were performed with no maternal or foetal deaths. Macafee and McClure⁴ corrected foetal mortality, all cases 6.10 per cent, primiparae, all ages, 10 per cent, multiparae, 3.42 per cent. The following authors give these corrected figures of foetal mortality in primiparae of all ages: Allan,⁵ 15.6 per cent, West-

man,⁶ 11.2 per cent, Bourne,⁷ 11 per cent, Pierson,⁸ 8.6 per cent, Dewar,⁹ 9.37 per cent, Marshall,¹⁰ 3.59 per cent, Roy,¹¹ 10.3 per cent, Moore,¹² 16.5 per cent, Hawker and Soule,¹³ 10 per cent

Goethals,¹⁴ using the following standards of maturity: premature, less than 5 pounds, immature, 5 to 6 pounds, mature, more than 6 pounds, gives the following figures over a very large series: Primipara, corrected foetal mortality: premature, 78.7 per cent, immature, 20.9 per cent, mature, 6.5 per cent. From 1913 to 1934, primiparae corrected foetal mortality 14.2 per cent

In a more recent paper Goethals¹⁵ gives the following figures: From 1888 to 1932, by the vaginal route, primiparae corrected foetal mortality, 10.2 per cent. By Caesarean section, 3.1 per cent. Since 1926 he has been performing breech extraction with the cervix fully dilated and his corrected figures are 7.4 per cent

Snoek and Canon,¹⁶ in a paper on breech delivery in primiparae over the age of 30, which is the group we are discussing, treated 11 conservatively, i.e. vaginally, with 8 stillbirths, and 11 cases by Caesarean section, with no foetal or maternal mortality. These various authors figures are given in the following table

Author	Corrected foetal mortality in primiparae of all ages (per cent)
Gibberd G F (Guy's Hospital)	28.0
Patton C D and Mussey R B	5.34
Vacafée C H J and McClure R I	10.0
Alan R M	15.6
Westman A	11.2
Dewar J B	9.37
Bourne A	11.0
Pierson R N	8.6
Marshall C M	3.59
Roy D	10.3
Moore J	16.5
Hawker, W H and Soule S D	10.0
Goethals T R (1913-34)	14.2
Goethals T R (from 1926)	7.4

The average foetal mortality from these

figures is 11.4 per cent. What relation do these figures bear to the foetal mortality in elderly primiparae? This is not easy to gauge accurately, but Nathanson,¹⁷ has stated that stillbirths are three times as high in this group as in the younger primiparae and multiparae. This would give a figure of somewhere in the region of 30 per cent foetal mortality. My own ratio, as will be shown later, is almost 5:1 elderly primiparae to all other cases. Siddall,¹⁸ at the Twelfth Annual Meeting of the Central Association of American Obstetricians and Gynaecologists stated that elderly primiparae have a lamentable foetal mortality in the region of 25 to 30 per cent

At Saint Mary's Hospital, Manchester, in the years 1932 to 1940 inclusive, 1,077 women with a breech presentation were delivered vaginally. The corrected foetal mortality in booked cases was 6.09 per cent and in emergency cases, 6.7 per cent. In the same period 145 were delivered by Caesarean section and 62 of these were primiparae of 30 years of age or more. From 1932 to 1941, inclusive, 128 primiparae of 30 years of age or above were delivered vaginally of a single foetus weighing 6 pounds or more, there not being any signs of foetal abnormality, maternal pathology, or other complications which might account for foetal death. All twins have been excluded, but not cases of mild toxæmia

One may assume, therefore, that in these cases any untoward happening to the child can be attributed to the delivery. Of these 128 deliveries 85 children were alive and survived, while 43 were either born dead or succumbed within a short time of delivery. This represents a foetal mortality of 33.5 per cent. There were 4 maternal deaths. Some degree of toxæmia was a contributory factor in two cases and mitral stenosis in one. The fourth fatality was ascribed to obstetric shock. In the same period, 62 women in the same group as

above were delivered by Caesarean section, with 1 maternal death (a patient with acute toxæmia) and no foetal death

With regard to the size of child that will stand the best chance of surviving by vaginal delivery, opinions seem to differ Higgins,¹⁹ in a recent paper, stated that in his opinion the most potent cause of foetal death was a large child, and for this reason he was in favour of induction of labour before term if necessary R S Siddall supports this by stating that breech babies of 8 to 9 pounds carry a 25 to 30 per cent foetal mortality Goethals, however, gives the following mortality figures by weight of foetus (all breech cases)

4½ to 5 pounds, 25 per cent, 5 to 5½ pounds, 20.4 per cent, 5½ to 6 pounds, 11 per cent, 6 to 6½ pounds, 10.3 per cent, 7 to 7½ pounds, 10 per cent, 7½ to 8 pounds, 6.4 per cent, 8 to 8½ pounds, 9.7 per cent, 8½ to 9 pounds, 9.3 per cent, 9 to 9½ pounds, 18.1 per cent, 9½ to 10 pounds, 22.2 per cent, over 10 pounds, 33 per cent

As can be seen, the weight with the lowest foetal mortality is the 7½ to 8 pounds group, and on both sides of this group the figure rises, but not really very significantly until 9 pounds or more, and 6 pounds or less My own experience has led me to believe that an average weight baby of about 7 to 7½ pounds will stand delivery best, and that premature induction of labour will not improve the foetal mortality figures

These factors are impressive and show that the "weight" factor must always influence our choice of the method of delivery Of other factors to be considered, the most important, in my opinion, is that in this particular group of women there are many who are not likely to have another child When one considers that to the vast majority of these women and their husbands the birth of a living healthy child will bring many years of great happiness and a new sense of completeness to their lives,

then no effort should be spared to bring about this felicitous result Heavy indeed is the responsibility of those in charge of these cases

By the vaginal route there is also the chance, admittedly not great, of a birth injury to the child, due either to manipulations in the delivery or to the rapid changes in shape of the cranial sphere Although the typical intracranial haemorrhages as described by Holland are either incompatible with life or are so small that recovery is said to be complete, nevertheless I do not know that any one has followed up a series of cases to show that they all remain symptomless in later life Though anatomically they cannot give rise to a cerebral diplegia (Little's disease) it is possible that other symptoms may manifest themselves Various other injuries have been encountered or described, among them being abdominal visceral injury, which is uncommon, fracture of the clavical and upper limb, dislocation of the shoulder (Petrignanni²⁰), Erb's palsy, combined brachial and phrenic palsy—Kofferath's syndrome (Melland²¹), fracture of the shaft of femur, according to Gibberd 5 per cent, separation of the lower femoral epiphysis (Burman and Langsam²²), and haematoma of the sterno-mastoid muscle, the visible sign of vascular damage leading to a congenital torticollis Admittedly the vast majority of these injuries can be easily and successfully treated, and I do not put them forward as a serious factor as compared with the foetal mortality

Finally, a factor which cannot be completely dismissed is that in this group of women there is an increased incidence of unpleasant sequelae, due partly to their age, partly to the increased incidence of interference and prolongation of labour I do not intend to enumerate these sequelae except to say that although obvious damage may not be visible, anyone who has per-

formed postmortem examinations after a prolonged labour and has seen the small haemorrhages and tears in the broad ligaments, Makendrodt's ligaments and other pelvic floor supports, can have but little doubt that they play some part in a future prolapse of the uterus.

Enough I hope has been written to show that the treatment of this group of women is far from satisfactory. How then can we improve this state of affairs? Either by an improvement in our technique of vaginal delivery to give comparable results with Caesarean section, or by adopting Caesarean section as the mode of delivery in nearly all cases. As regards vaginal delivery, Eden²³ in 1931 stated "The art of managing this particular type of difficult labour has not reached a point at which we can afford to rest content." This, I think, is equally true to-day.

Breech delivery as conducted by experienced obstetricians varies a great deal, but one can roughly divide it into two classes. Firstly, there is the conservative school who, whether the legs are extended or not, are content, either with or without an episiotomy, to guide the breech over the perineum, merely assisting the birth of the legs, and to bring down the arms as the scapulae become visible. The head in ordinary cases is born by natural forces or aided by fundal pressure, except where difficulty is encountered when the forceps are applied to the aftercoming head. I know of few better figures than those of Burns²⁴ and Marshall except those of Hansen²⁵ who from 126 deliveries in private practice, of various ages and parity, had a corrected foetal mortality of 0.8 per cent. Admittedly this is not a large series and, as was pointed out in the discussion following his paper, others have had an almost equally low figure over this number of cases, but not over a larger series. These all belong to the conservative school.

Then there is the active school, the advocates of which either perform an extraction when the cervix is fully dilated—Goethals—or at least bring down a leg or legs if extended and possibly also flex the arms *in utero*. Such an authority as Bourne²⁶ is prepared to do this. Figures as good as the average and almost as good as the best in the conservative school have been produced by this active intervention, and when one reflects that these are all obstetricians of experience who have almost certainly tried both methods, then one cannot help but agree with Gibberd that it is probably not the method but the individual skill of the obstetrician that produces good results.

In Manchester the usual practice is a conservative delivery based on the method of the Liverpool school, as described by Burns and Marshall, with slight modifications but adhering closely to Burns technique in the delivery of the head. In my opinion, episiotomy is essential in all primiparae, and the majority of multiparae, as I have pointed out previously⁷ and a large number of others have given it their approval—Marshall, Dewar, Randall,²⁷ Pieri,²⁸ Mazenek,²⁹ Kretzschmar and Huber³¹ and Higgins.

As regards Caesarean section, in the Saint Mary's, Manchester series there were 62 cases with no foetal death. Brindeau and Lantuetoul³² describe certain cases of breech presentation, chiefly primiparae, who were operated on in Tarnier's clinic late in labour without a foetal or maternal death. Indications for Caesarean section in breech presentations are suggested by other writers (Anderodias and Pery,³³ Meyer,³⁴) but I have not encountered previously any who would recommend its almost routine use in a primipara 30 years of age or more.

Nothing is more salutary than a sane conservatism in any branch of medicine, but it must be in accordance with the patient's

best interests. Surely our function is to assist our patients in retaining a healthy body and so having a healthy and happy mind. Few procedures can give such happiness as the birth of a healthy baby in these cases. Until the figures for foetal mortality by the vaginal route can compare with Caesarean section, and I have some doubts if they ever will as there are so many unpredictable factors, then I think Caesarean section should be the choice in the vast majority of these cases. Even Potter,³ in a discussion on Goethal's paper, stated "In women who are past 35 or 40 who have never had a child and will probably never have another, we lean to the operative side, that is Caesarean section."

There is little difference in the maternal mortality for either type of treatment, as since the introduction of the lower segment Caesarean section, and possibly in certain cases the judicious use of the extraperitoneal operation modified on Latzko's technique, the maternal mortality figures in the hands of competent surgeons have been in the region of 1 per cent. To clarify our views on this subject it is interesting to see how the matter could be put to the patient in simple language.

By Vaginal Delivery

- 1 The chances are only 2 to 1 on your child being born alive
- 2 There is a slight risk of injury to your child
- 3 There is the possibility that trauma to yourself may have unpleasant after-effects
- 4 The risk to your own life is about equal to the risk by abdominal delivery

By Caesarean Section

- 1 You have probably less than a 1 in 50 chance of losing your child's life

- 2 It involves an abdominal operation, but the risk to yourself is not more than 1 in 100
- 3 The chances of injury to your child are negligible, and of unpleasant sequelae to yourself certainly no more than by the vaginal route

Finally, by either method, this may well be your only chance of having a child.

If these conclusions are true, what then should be our conduct of these cases? For the general practitioner I would suggest that these cases be placed under the care of an obstetrician and never be treated at home. Rosenfeld⁴ has aptly said "A woman in labour whose infant presents by the breech is entitled to the services of an experienced obstetrician." I would not infer from this that there are no experienced obstetricians in practice, but I would amplify Rosenfeld's statement and suggest that she is also entitled to the very best conditions. Even if I agreed with vaginal delivery, I do not think that the patient's own home is a place where a difficult delivery can be carried out by the standards of modern obstetrical technique.

For the obstetrician I would suggest that the usual clinical examination be carried out and unless there is any contra-indication an external version should be attempted at the appropriate time. If this fails, however, there should be a very thorough and critical review of the case. The patient's history must be thoroughly gone into with particular attention to the following points. Did she marry late in life, or did she marry early but only recently conceive? If of the second group, is there any reason for this late conception and has she been attending a gynaecological clinic for sterility? From an investigation of these points a rough estimation can be made of her chances of having further children. Then a very full clinical re-examination must be made, supplemented

by a radiological examination. This should supply evidence as to the state of the child and the adequacy of the maternal pelvis. Radiographs must be taken at least in the dorsal, prone and lateral positions and supplemented where necessary by stereographs.

The final result of all these investigations should be an assessment, firstly of the size and state of the foetus and whether there is any suggestion of foetal abnormality, secondly of the size, configuration and inclination of the maternal pelvis, thirdly, of the relation so far as one can judge between the child and the maternal pelvis, and finally of the patient's chances of having further children. In the present state of our knowledge none of these factors can be estimated with certainty, but a reasonably reliable impression can be gained.

In the decision as to which method of delivery should be adopted, I would say that if, as far as can be judged, the foetus is normal and healthy, then only in those women in this group under 35 years of age, and whose pelvis is obviously adequate, when there are no other contra-indications and when there is a good prospect of further children, should the vaginal route be adopted.

There are too many unpredictable factors such as uterine action and deflexion attitudes of the foetus, and the stakes are too high for much risk to be taken. If we rigidly adhere to these criteria then, in my opinion, the number of primiparae delivered vaginally will be very small. By Caesarean section, in this group of women, we are almost assured of a happy result, but during vaginal delivery the spectre of death of the child sits constantly at the elbow of the accoucher, alert for any abnormality and quick indeed to take advantage of the slightest hitch in the smooth technique of delivery.

If any further justification were needed

for this somewhat radical attitude, I think it would be this. If operation is carried out, as it often is, possibly rightly, for such non-fatal diseases as so-called chronic appendicitis, subserous fibroids, with few if any symptoms and accidentally discovered ovarian cysts, then surely it should not be withheld from a woman whose only chance it may be to enjoy the supreme fulfilment of her life.

CONCLUSIONS

1. Two similar series of cases of breech presentation in primiparae, of 30 or more years of age, from Saint Mary's Hospital, Manchester, during the last decade, have been investigated. Those delivered vaginally had a 33.5 per cent foetal mortality, while by Caesarean section there was no foetal death in 62 cases.

2. Some of the more recent literature is reviewed, and in view of the discrepancy in the results between the two methods of delivery, a plea is made for a more widespread use of Caesarean section in these cases.

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JOURNAL OF OBSTETRICS AND GYNAECOLOGY

Pregnancy and Labour in a Case of Intrapelvic Protrusion of the Acetabulum

BY

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INTRAPELVIC protrusion of the acetabulum is an uncommon condition first recognized and described by Otto¹ in 1824, his case being found in a pelvis in an anatomical museum. Its rarity is shown by the fact that only 106 cases were collected from the literature by Sloane and Sloane² in 1937. Many articles, under different titles, have been published on this condition. These are found chiefly in the German literature, while more recently, following Hertzler's³ article in 1922, a number have been published in the American journals. The following case of pregnancy in an "Otto pelvis" is considered worthy of record.

CASE RECORD

Mrs M T, aged 26, a primigravida, first attended St Mary Abbots Hospital Antenatal Clinic on June 25th 1941.

Personal History At the age of 15, 3 months after a fall from a bicycle, she was admitted to hospital for treatment of a painful lump. For 18 months she was kept in plaster of Paris and for 8 months was treated by a calliper iron. Since then she had stiffness of both hips unaccompanied, however, by pain. There was no family history of hip joint disability. Apart from scarlet fever in infancy there were no other illnesses.

Obstetric History The last menstrual period was on February 6th 1941 and the estimated date of

delivery was November 13th 1941. There was no history of vaginal discharge and there were no abnormal symptoms. The hip condition had not altered during pregnancy.

General Examination She was a fairly well built woman of normal nutrition. There was no anaemia. Some of the teeth were carious and dental treatment was prescribed. The throat and pharynx were normal and the breasts and nipples were of normal development. Nothing abnormal was found on examination of the heart and lungs. The blood-pressure was 110/60, there was no oedema of the ankles and the urine was acid and did not contain any albumin or sugar.

Obstetric Examination The uterus corresponded in size to 20 weeks pregnancy. External ballotement was present but the foetal heart was not heard. Both hip joints showed marked limitation of movement. Flexion was reduced to about 45 degrees and hyper-extension was impossible. Abduction and external rotation were almost completely lost. The lumbar spine showed some lordosis. The external pelvic measurements were: Interspinous diameter 10 inches, intercrural diameter 11 inches, external conjugate $8\frac{1}{4}$ inches and transverse of outlet 4 knuckles diameter.

On vaginal examination there was no evidence of past or present inflammation. The promontory of the sacrum could not be reached. On either side a smooth protrusion was palpable at the acetabular level. The sacrum was normal and the sacrospinous notches easily admitted 2 fingers. The size of the outlet was adequate. Internal ballotement was elicited.

X-Ray examination demonstrated a typical Otto pelvis. Both hip joints showed narrowing of the joint space and deepening of the acetabula which were protruded inwards more especially on the left side. The acetabular floor was thinned. Osteophytic outgrowths were present arising from the margins of the femoral heads, and there was a moderate degree of coxa vara.

The Wassermann Kahn and gonococcal fixation tests were negative.

Subsequent Progress. The patient attended the Clinic regularly. The blood-pressure remained within normal limits and the urine showed no abnormality. No abnormal symptoms developed and she did not complain of any change in the hip condition or of backache. On October 1st, 1942, the uterus corresponded in size to 34 weeks pregnancy. The presentation was a vertex, the foetus lying in the left occipito anterior position. The head was engaged in the pelvis, and the foetal heart was heard. There was no change in presentation or position during the remainder of the pregnancy.

Labour. She was admitted in labour at 10.30 p.m. on October 10th, 1941. Pains had begun at 8.30 p.m. On examination the position was still the same with the head deeply engaged. Nothing abnormal was found and rectal examination showed the cervix to be 2 fingers dilated. The membranes ruptured spontaneously at 11.45 p.m. the cervix was fully dilated at 12 midnight and normal delivery of a living male infant took place in the left lateral position at 12.40 a.m. The infant weighed 7 pounds 4 ounces, its length was 21 inches, and the circumference of its head 13½ inches. The placenta and membrane were delivered complete at 12.55 a.m. without abnormal postpartum loss. The cord was 22 inches long and inserted centrally on the placenta. A small laceration of the posterior vaginal wall was present and was repaired by catgut. The temperature was 98.4°F, the pulse-rate 90 and the respiration rate 20 at the conclusion of the labour. The total duration of the labour was 4 hours 25 minutes.

Puerperium. This was apyrexial and uneventful. Vaginal examination before discharge showed that the uterus was anteverted and involuting normally, the cervix healthy and the pelvic floor sound. Further X-Rays of the pelvis did not show any change since the previous films. Mother and

infant were discharged on November 10th 1941. The infant which was breast fed 3 hourly, weighing 7 lbs 13 ounces.

DISCUSSION

Cases of intrapelvic protrusion of the acetabulum have been grouped as typical and atypical. Henschen¹ suggested that in a typical case the inner wall of the acetabulum protrudes into the pelvis, and the acetabular cavity is enlarged, especially upwards and inwards. The head of the femur, which is essentially normal in contour, is displaced into the deepened acetabulum and produces a shortening of the limb. The radiological appearances are well described and illustrated by Doub² in a review of 8 cases. The changes in the acetabulum are most striking. There is a very definite thinning of the medial and inferior wall with a dome-shaped protrusion of this into the pelvis varying from a few mms to cms. The thin acetabular wall is thicker in its upper part, and narrows as it progresses downwards. Considerable eburnation is seen. The head of the femur is typically intact and is deeply buried in the acetabulum. It may have a slightly elongated appearance, but the integrity of the femoral head is an essential characteristic. Osteophytes often project outwards at the junction of the head and neck, and some degree of coxa vara may be present. The head of the femur being deeply buried in the acetabulum, it follows that the great trochanter is closer to the ilium, this, and the presence of osteophytes, effectively limit movement of the joint. The case described in this paper fulfils the above postulates of a typical case.

The condition is usually found in the middle-aged, and is twice as common in females as in males. Analysing 79 cases Pomeranz³ found that 47 were in females. The condition was bilateral in 29 cases. A number of cases have been published in



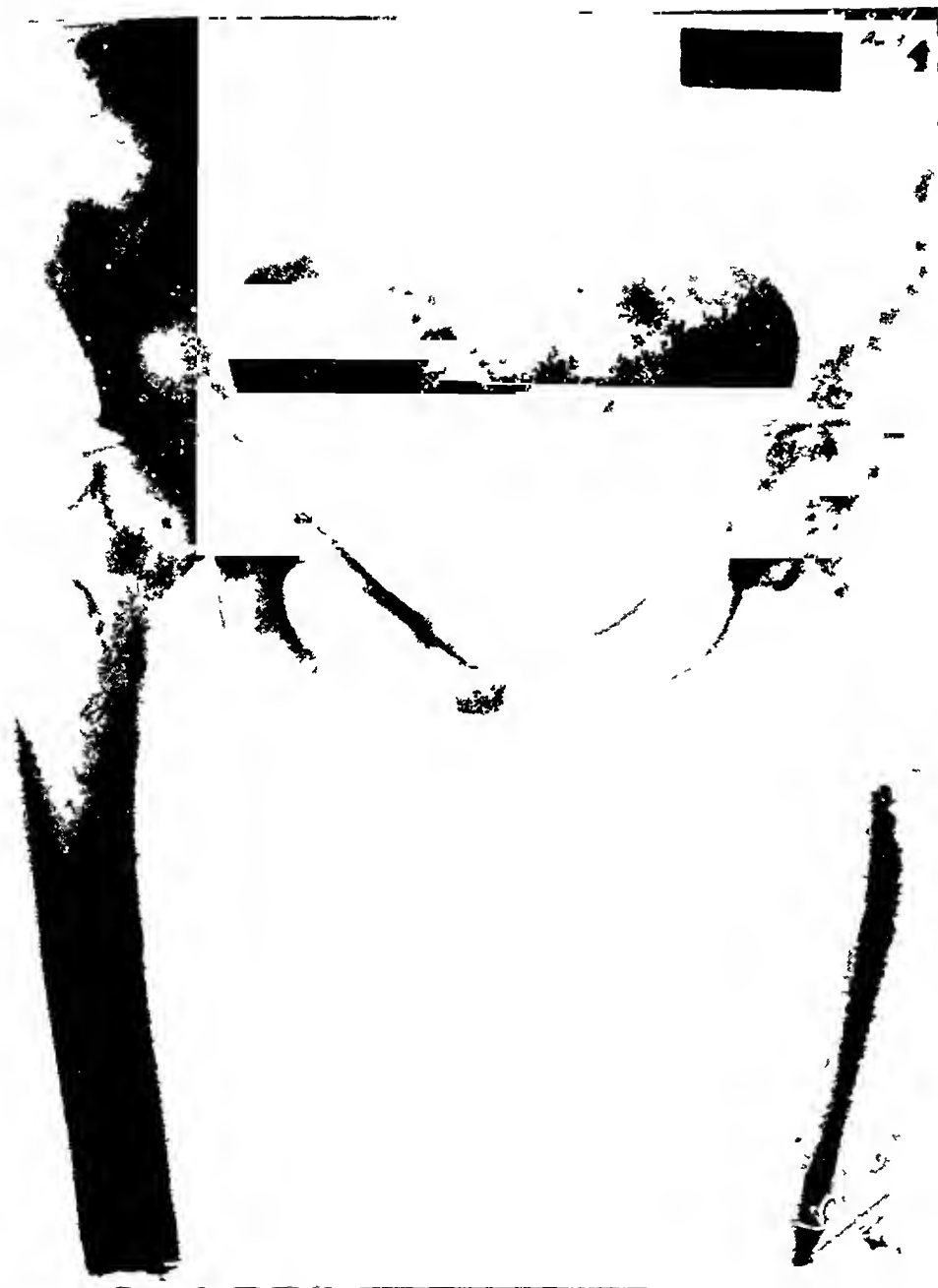
Fig. 1 Before Delivery

393E=



FIG 2 After Delivery

00271 R



C

FIG 3 After Delivery

which a family history of hip joint disability has been present, and it is quite possible that heredity may be a factor in the aetiology. There is no evidence of this in our case.

Much has been written on the causation of this condition since it was first described by Otto who regarded it as a manifestation of abnormal gout. Saupe⁷ gives a long list of possible causes and special influences including trauma, faulty posture, kyphosis, spondylolisthesis, osteitis deformans juvenilis, osteomalacia, polyarthritis, gonorrhoea, tabes, tuberculosis, and tumours. Cases due to echinococcosis have even been described. It would appear to be preferable to regard the condition as a clinical syndrome rather than a disease entity. The causation appears to be due to a localized weakening or destruction of the acetabulum which yields to the boring pressure of the normal femoral head. Pomeranz,⁶ who divides his cases into acute and chronic types, holds that "the Otto pelvis is an atypical but essentially non-specific arthritis of the hip joint."

Golding's⁸ classification is worthy of consideration. He divides such cases into three groups: (1) Caused by growth disturbances; (2) Rheumatic group: (a) specific (gonococcal) infections; (b) non-specific infections; (c) metabolic arthritides; (3) Group including many varieties due to gross destructive disease. Considering the first group the acetabulum is developed by the union of the three pelvic bones by means of a triradiate cartilage in which centres of ossification appear about the 12th year. Union occurs about the 16th to 17th years. Eppinger's⁹ hypothesis considers the Otto pelvis to be due to a disturbance of growth affecting this triradiate cartilage. Schaap¹⁰ believes the condition is due to a congenital deformity of the acetabulum while Rechtman¹¹ goes further and maintains that the aetiology of all

typical cases is primarily a congenitally deep acetabulum resulting from overgrowth of some element in its development. He maintains the protrusion is an acquired defect superimposed on a deep acetabulum, symptoms only appearing after some trauma or infection has aggravated the condition. So called typical cases are usually bilateral. The case reported above would fit into this group: the initial symptoms appeared at the age of 15 following trauma, and the condition was bilateral. A gonococcal origin has been stressed by Schlagenhauser,¹² Henschen,⁴ Keinbock,¹ and others. Sloane and Sloane² describe a case of acute Otto pelvis in a girl 18 years of age in which X-Rays demonstrated the onset and rapid development of the acetabular protrusion. The case was proved pathologically to be of gonococcal origin. Out of their 106 tabulated cases, however, only 13 were assumed or proved to be a result of gonorrhoea. In our case there was no evidence of gonorrhoea.

Benda¹¹ draws attention to the fact that the Otto pelvis if severe may cause serious obstetric difficulties, and Caesarean section may even be necessary. There is undoubtedly narrowing of the pelvis in bilateral cases and asymmetry in unilateral, but in our case obstruction did not occur, and it was felt that difficulty in delivery, if any, would arise mechanically from the limitation of movement of the hip joints. This, however, did not occur. Further, some of the published cases have borne children without difficulty, despite the fact that their symptoms would lead one to believe that the condition was present long before its radiological discovery. It would appear that, as in the pelvis associated with congenital dislocation of the hip, difficulty in delivery is not usually to be expected. The rarity of these cases and their usual onset in the middle life would also explain why little or no notice of this condition as a

cause of obstruction in labour has been taken. In our case pregnancy did not produce any exacerbation of symptoms and the X-Ray appearances following parturition were unaltered.

Symptoms in cases of Otto pelvis are those of a slowly progressing painful coxitis, and limitation of movement, particularly abduction and external rotation, is marked. Shortening occurs in unilateral cases. The intrapelvic protrusion can occasionally be felt *per abdomen*, and is usually easily palpable *per rectum* or *vagina*. Treatment is seldom mentioned in the literature. Early cases should be treated by prevention of weight bearing, while in late cases, apart from conservative measures, an arthrodesis on one side may be necessary if there is little movement and pain is disabling. Berg¹⁵ recently describes a case treated successfully by arthroplasty employing a vitallium cap, while in some cases an acetabuloplasty as described by Smith-Petersen¹⁶ might be indicated.

SUMMARY

- (1) Pregnancy and labour in a typical case of intrapelvic protrusion of the acetabulum is recorded.
- (2) The aetiology of the condition is reviewed.
- (3) The bearing on childbirth is considered.

ACKNOWLEDGEMENT

I would like to thank Dr W. Allen Daley, M.D., F.R.C.P., D.P.H., Medical Officer of Health, London County Council, for permission to publish this report.

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A Case of Pseudohermaphroditism

BY

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THE adrenocortical syndrome is characterized by sexual abnormalities discovered at birth, sexual precocity, reversion by pubescent and adolescent girls to the male bodily figurement, amenorrhoea, hirsutism, obesity of the face, neck and trunk, and hyperglycaemia, as well as cutaneous changes such as coarseness of texture and acneiform eruptions

These changes can be produced by hyperplasia or tumours of the adrenal cortex. This can be substantiated by the reversion to normal of the patient's condition after removal of a cortical adenoma

Werner¹ suggests a simple classification of adrenocortical syndrome in which the condition occurs in three periods which obviously are not distinct from each other, and which show definite gradations with age as follows

TYPE NO 1 Cortical disturbance occurring in embryonal foetal life producing pseudohermaphroditism. The external genitalia do not show clear cut male or female differentiation. There are all gradations of development and it may be extremely difficult to know the sex of the individual

TYPE NO 2 Prepubertal and adolescent cortical hyperfunctions (hyperplasia or tumour) producing pubertas precox in the child, with accentuation of the male characteristics in the male, and with a tendency towards masculinization in the female, characterized by enlarged clitoris, hypertrichosis, masculine voice, develop-

ment of male bodily configuration and absence of menstruation at or after puberty

TYPE NO 3 Adult cortical hyperfunction (hyperplasia or adrenal neoplasm) causing masculine type hypertrichosis and amenorrhoea frequently associated with obesity

Adopting this classification the case reported here would appear to be an unusually good example of Type No 1

HISTORY

J R consulted me in September 1942 because of her general appearance and 'a condition in the vulva region'

The patient was aged 18 and noticed that about 3 years ago hair commenced to grow all over her face, but particularly on the upper lip. This condition has gradually become more pronounced. Shaving has been resorted to for the past year and is now necessary about twice a week. She noticed also that her external genitals were not normal and that there was complete absence of breast development. Menstruation had never occurred.

The patient is particularly healthy and the only illness suffered was measles. Her father and mother are both alive and well as also are her 3 brothers and 2 sisters who are perfectly normal physically although none are married.

The patient is an exceptional athlete, has won many athletic competitions and is capable of covering the 100 yards in 11.5 seconds. She plays hockey for her school which has won the Senior Schools trophy in Leinster, and I understand she is the outstanding player.

Psychologically she appears perfectly normal for her age. She has her natural female friends and enjoys going to dances.

Examination of the patient revealed a rather small adolescent girl about 4 feet 9 inches in height. The hirsuties on the face was easily noticeable and her voice was of low pitch. Her skin was rather coarse and there were a few acne spots on the back but nothing noteworthy. Further examination showed the physical structure to be characteristically male with large square shoulders, small pelvis and very well developed arms and legs. Hirsutism was generally present but the pubic hair was of female distribution. Female development of the breasts was absent and the nipples were small. The vulva was present to the extent of the labia majora but the labia minora were absent. A well formed clitoris 1½ inches in length was present and the opening of the urethra was just below it. The vagina was completely occluded. Swellings indicating the presence of testicles could not be felt in the groins.

X ray examination

Pituitary fossa Within the limits of normal

Skull Within the limits of normal

Kidneys Films taken 5, 15 and 20 minutes after injection of Uroselectan show function in both kidneys to be good with a double ureter and pelvis on the left side. Calices of both kidneys within the normal limits. It was not possible to demonstrate any undue enlargement of the suprarenal glands and there is no displacement of either kidney.

Pelvis Of male type

Urine Specific gravity 1018. Acid. no albumin, no sugar or acetone, no pus, blood crystals or casts.

Urmay hormone excretion The patient in two separate consecutive 24 hour specimens of urine excreted the enormous amounts of 125 and 109 mg of 17 ketosteroids. Anything over 40 mg is highly significant of either an adrenal tumour or gross hyperplasia. She also excreted 36 mg of sodium pregnandiol glycuronide in a 24 hour specimen. This figure is comparable to the amount which might normally be found in pregnancy.

Recently Patterson⁷ has shown that the ketosteroid output indicates very high excretion rates. At a pre-pubertal age it is impossible to differentiate between adre-

nal hyperplasia and an adrenal tumour solely on the basis of the ketosteroid output.

Blood Normal 1 e, haemoglobin (Sahli), 95 per cent red-blood cells, 4 800 000 per c mm. Whites 9 800 per c mm. colour index, 1.0

Differential count Polymorphs 69 lymphocytes 22 monocytes 7 eosinophiles 1, and basophiles 1

Red cells normal in size and shape

Blood sugar 110 mg per 100 c c

urea 24 , ,

calcium 9.7 , ,

cholesterol 120

On October 15th 1942 laparotomy was performed. Inspection of the pelvic organs disclosed an infantile but formed uterus with normal ligamentary attachments all equally underdeveloped. The Fallopian tubes were also normal but very small. A large oval shaped ovary was situated on each lateral pelvic wall and did not show any evidence of ovulation having ever occurred. The adrenals were palpated and did not contain any abnormal tumour but appeared to be considerably larger than normal. As the appendix contained several concretions it was removed and a small piece of the right ovary was removed for microscopic examination. The abdomen was closed and an attempt was then made to demonstrate the presence or absence of a vagina. A metal catheter having been inserted into the urethra the tissue below it was incised to a depth of about 2 inches but evidence of a vagina could not be found.

Postoperative convalescence was uneventful except for retention of urine during the 1st week.

Examination of the piece of ovary showed normal stroma containing a small follicular cyst. There was no evidence of corpora lutea or corpora albicantes. In the cortical portion were numerous primordial follicles.

Before leaving the nursing home the patient was told that she was a female, but that marriage would be inadvisable, as she could never menstruate, still less could her marriage be consummated. She desires to take up medical studies and this was strongly encouraged.



E S



ES

OVARY

CONCLUSIONS

1 A case of pseudohermaphroditism has been presented

2 The condition was due to bilateral hyperplasia of the adrenal cortex and started in embryonal foetal life

ACKNOWLEDGMENTS

I am very indebted to Dr J Freedman, who first recognized the abnormalities present, to Dr Gerald Dockeray for his general examination and all the blood and

urine investigations, to Dr J C Cherry for his assistance at the operation, particularly for his examination of the adrenals, to Dr T Bradshaw for his urinary hormone excretion investigations, to Dr D O'Farrell for his X-ray reports, and to Dr R. W Shaw for giving the anaesthetic at the operation

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Torsion of Pregnant Uterus

BY

W. JONAS, M.D. (Heidelberg)

PATHOLOGICAL torsion of the uterus during pregnancy seems to be a rare complication. The obstetric textbooks—if at all—mention it briefly. On the other hand, diagnosis of the condition, which should be made early enough to assure the proper and timely treatment, generally evades our recognition. It is for these reasons that it seems justifiable to report on one such case.

CASE HISTORY

The patient, 30 years old, pregnant for the first time, menstruated last on March 20th, 1942. A pregnancy test, performed in May, was positive. She complained of slight backache and frequency of micturition until July 4th when she suddenly commenced to bleed, and it was for this reason that I was called in on July 5th.

As a child, before puberty, she had suffered from colitis. Her menstruation commenced at the age of 14 years and had been regular, but the loss was scanty. She had suffered from backache which 2 years ago led her to consult a gynaecologist on two occasions. A retroflexed uterus was found and operative treatment was suggested with particular regard to possible future pregnancies.

She was now complaining of pain, spreading from the middle of the lower abdomen to the left breast, slight giddiness and increasingly frequent micturition so that during the night she had sometimes to get out of bed four or five times.

The general condition of the patient was good, her complexion healthy, her tem-

perature normal, the pulse strong and slow. The blood-pressure was 110/70 and the urine free from albumin and sugar.

On examination, the abdomen was soft and there was no tenderness. The fundus uteri which should have been at the level of 3 fingers above the symphysis pubis could not be felt.

On vaginal examination, there was slight loss of fresh blood from the vagina. It was hardly possible to reach the cervix uteri which lay high up behind the upper border of the symphysis. The external os was closed. A soft tumour, apparently directly connected with the cervix, filled the pouch of Douglas. Its size corresponded to that of a pregnant uterus of 4 months duration and appeared to be a pregnant organ fixed in backward displacement. Both uterosacral folds were felt as tight cords.

After passing a catheter, which proved that there was no retention of urine, the examination was repeated with the patient under ether anaesthesia in order to attempt to replace the uterus. This attempt was unsuccessful and I gained the impression that adhesions prevented the liberation of the uterus, but, when the abdominal walls were relaxed, I could feel a projection arising from the anterior wall of the uterus which was of harder consistence and the size of a fist.

A diagnosis of retroflexion of a 4 months pregnant uterus with sacculation of the anterior wall, was made, despite the fact that it was rather early in the pregnancy for the formation of a sacculation. A pos-



sible malformation of the uterus could not be excluded

It was decided to keep the patient under observation for the following reasons

Her satisfactory general condition

The very slight degree of bleeding

The apparent presence of sacculation and the refusal of the patient to undergo an operation

Daily injections of corpus luteum hormone were administered and the bleeding stopped for a few days but recommenced, and on July 26th the haemoglobin was only 50 per cent. A second opinion was obtained and operation was urgently recommended

Operation was performed on July 30th under gas-ether anaesthesia. After opening the peritoneum in the middle line the uterus presented in the wound and one ovary, Fallopian tube, and a poorly developed round ligament were seen to be close to the right border of the incision. The other appendages were not found. Another tumour could be felt in the depth of the pouch of Douglas which was slightly larger than the first. It was of a blueish-red colour, separated from the other by a shallow arcuation. It was fixed by thin adhesions which could easily be separated. When this tumour was lifted up it had to be twisted clockwise by 90 degrees before the left appendages could be seen. These were fixed with the tumour in the pouch of Douglas. It was then evident that the condition was caused by torsion to the left of a bicornuate uterus by 90 degrees, the actual site of the torsion being the lower uterine segment, and that its left horn, which contained the pregnancy, was fixed in the pouch of Douglas.

To prevent a recurrence of the torsion, the round ligaments were shortened by duplication.

The first days after the operation were uneventful. Bleeding decreased. On the

5th day the membranes ruptured and a foetus of 6.5 inches was expelled. As the bleeding then increased it was necessary to separate the placenta, which was attached to the left wall of the left horn. The patient recovered quickly and was discharged on the 19th day following the operation.

PATHOLOGY

In discussing the factors responsible for the origin of a pathological torsion, a distinction must be made between predisposing and initiating causes. In determining the last mentioned in the first instance, there are several theories put forward to explain the mechanism of torsion as it occurs in pedunculated organs or tumours which may be applied to the pregnant uterus. There is a consensus of opinion that the transmission of body movements plays an important part in activating the torsion. Contractions of abdominal muscles or the filling degree of neighbouring organs, that is, bladder and intestines, might contribute to this mechanism. Cases taken from veterinary obstetrics in which torsion of the pregnant uterus is not infrequent, confirm this conception. In actual fact, the condition was first described by an Italian veterinary surgeon in the year 1662. It would appear, however, that the importance of the intrinsic muscles is overlooked, particularly in this case of retroverted partially fixed bicornuate uterus where it is possible that the contractions of the non-pregnant horn might have been the main activating factor, just as in self-replacement of a retroverted pregnant uterus, contractions of the muscular organ as well as the enlargement of the uterus are the main factors responsible for the eventual forward position.

In considering the predisposition to torsion, X-ray photographs taken after utero-salpingography with Neo-Hydriol

give a satisfactory explanation. They show the retroverted bicornuate uterus 3 months after the operation, and give an idea how narrow and elongated the cervix is compared with the width of the bicornuate body. Taking into account the softening of the lower segment during pregnancy and the poor development of the muscular and fibrous attachments, it is evident that this abnormal, unilateral uterus shows a high degree of mobility. In addition, the haemodynamic principle may have played a certain part in the mechanism of the rotation owing to the special conditions of the blood supply and the vascular changes associated with pregnancy taking place in the larger pregnant horn. The adhesions which fixed the pregnant horn within the pouch of Douglas were yet another factor contributing to the condition of torsion.

DIAGNOSIS AND TREATMENT

The correct diagnosis of this case was not made before the operation. Apart from the special condition of backward displacement, which was misleading, the reports of all cases published so far show that torsion of the pregnant uterus is very seldom recognized before it is proved by operation. This fact is probably due partly to the apparent infrequency of the complication, but chiefly to the lack of characteristic symptoms. Differential diagnostic deliberations which had to be considered and excluded in our case were

Ectopic pregnancy

Pregnancy with ovarian tumour impacted in pelvis

Retroflexion of pregnant uterus with fibroid in the anterior wall

The bleeding apparently was not due to a premature separation of the placenta, as

the manual removal of the placenta proved, but was caused by the venous congestion.

The importance of uterus-torsion should not be under-estimated when it is realized that an exaggeration of the physiological dextro-rotation or a pathological torsion may be involved in some cases of threatening abortion, attacks of abdominal pain during pregnancy and premature separation of the placenta, particularly if the uterus contains fibroids or shows any other abnormality of its shape. This is reason to attribute more importance to this complication.

Although surgical interference in this case was delayed not only by the refusal of the patient, but also by the fact that certain signs seemed to indicate the possibility of self-correction, it should be emphasized that in every case of suspected torsion, surgical treatment is necessary. A few cases are reported in which spontaneous rectification took place, or replacement under anaesthesia was successful, but it is very doubtful whether these cases actually belonged to the category of a pathological uterus-torsion.

SUMMARY

A report is given of a case of pathological torsion in a retroverted bicornuate pregnant uterus.

The mechanism of torsion, its diagnostic difficulties and the treatment are discussed.

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Chromophobe Adenomata of the Hypophysis Cerebri

BY

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(Flight-Lieutenant, R A F V R)

IN a series of 50 hypophyses examined macroscopically and microscopically 6 adenomata of chromophobe type were discovered. None of these adenomata had been diagnosed clinically.

REVIEW OF LITERATURE

In reviewing the literature I was struck by the comparatively little attention that has been paid to these adenomata. There is, however, one admirable report of an investigation into these tumours by Norman M. Dott and Percival Bailey¹ working in conjunction with Harvey Cushing. Their study was the result of a review of clinical records of 162 cases with verified hypophyseal adenomata correlated with histological examination. They state that

The chromophobe adenoma is associated with evidence of glandular insufficiency. It is by far the commonest tumour, our series containing 107 examples. On a structural basis two types are perhaps deserving of mention. (1) Those in which the columnar structure of the normal hypophysis is maintained in greater or lesser degree. (2) Those consisting of a mass of cells without architectural arrangement and containing very little connective tissue stroma.

Loewenstein² who has made a careful study of the site of origin of hypophyseal adenomata, states that

They are encountered most frequently in one of three situations in early stages of their development: (1) In the pars intermedia. (2) in the periphe-

ral part of the pars distalis and (3) in the vicinity of the stalk (pars tuberalis). It is in these parts that the chromophobe cells predominate and the fact that they are embryologically the least highly differentiated cells of the hypophysis perhaps explains both the frequency with which adenomata originate in these places and the predominance of the chromophobe type of tumour.

Dott and Bailey found that hypophyseal adenocarcinomata are rare, and they are of the opinion that "possibly the chromophobe cells, being less highly specialized forms, are more prone to malignant transformation than are the eosinophilic or basophilic elements."

PERSONAL OBSERVATIONS

Six adenomata were observed. Five of these were chromophobe, and one was adenocarcinomatous. The age of incidence varied from 36 to 72 years.

Adenoma A

This tumour was found on horizontal section of the hypophysis. It was white in colour (photograph A1) and measured 7 mm \times 8 mm, while the hypophysis itself measured 15 mm \times 13 mm \times 10 mm. Microscopically, the tumour consisted of typical chromophobe cells with scanty cytoplasm, poorly developed cell wall, and vesicular nuclei. There was an attempt to form columns and groups of cells which were supported in a well marked reticular tissue (photograph A3).

Adenoma B

On horizontal section of the hypophysis a greyish area 2.5 mm in diameter was seen close to the pars intermedia. This corresponded microscopically to an adenoma (photograph B2) chromophobe in type, showing little attempt to reproduce the architectural arrangement of the anterior lobe.

Adenomata C, D and E

These were recognized only on microscopical examination of sections of hypophyses (photographs C₁, D₁, E₁). Adenoma C (photograph C₂) showed the best attempt by any of the adenomata to imitate the normal structure of the anterior lobe of the hypophysis.

Adenoma F

This tumour measured 7 mm × 12 mm × 10 mm, and the hypophysis itself measured 15 mm × 20 mm × 10 mm. Microscopically the adenoma was diagnosed as being of a malignant chromophobe type (photograph F2).

A striking feature of all these adenomata is the lack of capsulation of the tumour, yet there is, both macroscopically and microscopically, a definite edge where normal anterior lobe tissue ends and tumour tissue begins. This is well seen in the accompanying photographs. The photograph E₁ at first suggests that the adenoma has a definite fibrous capsule, but this is explained by the section's passing through the anterior lobe at a point where the tumour has grown outside, and come to overlap that lobe.

DISCUSSION

I attempted to associate the presence of these adenomata with signs of hypophyseal malfunction. The medical histories, clinical findings, and postmortem reports of each case were scrutinized for any fact

that might suggest a diminished functioning of the hypophysis. No single feature was found that would have led to a diagnosis of the presence of these adenomata during life. Further, each hypophysis was sectioned serially, and examination did not show any difference in microscopical appearance, apart from the presence of the adenoma, in comparison with the appearances presented by a whole series of normal hypophyses similarly examined. Indeed, adenoma D (photograph D₁) was found in the hypophysis of a woman who died of pneumonia 5 days after labour, and this hypophysis showed the usual physiological enlargement of the pregnant state. The relevant questions to be answered are: Do the adenomata here described, apart from the malignant one, represent a quiescent state in the cells of the anterior lobe, or are they early stages of growths that would have given rise to clinical manifestations had the patients lived? The first part of the query is prompted by the fact that chromophobe cells give rise to the eosinophil or basophil cells, and that the process may be reversible.^{1,4} Moreover, de Beer has shown that a "basophil area," similar in all descriptions to a basophil adenoma, occurs in the normal anterior lobe of the hypophysis of the ox, so that there may be such a thing as a "normal adenoma." The absence of associated clinical manifestations supports this idea. But the 6 adenomata described do not show the normal architectural arrangement of the cells of the anterior lobe, and one has undergone malignant change. For this reason they must be regarded as true tumour formations, in an early stage because of the absence of related clinical features.

SUMMARY

1. Six chromophobe adenomata of the anterior lobe of the hypophysis are described.



A1 Hypophysis cut in half horizontally
Whitish area shows adenoma x 1'

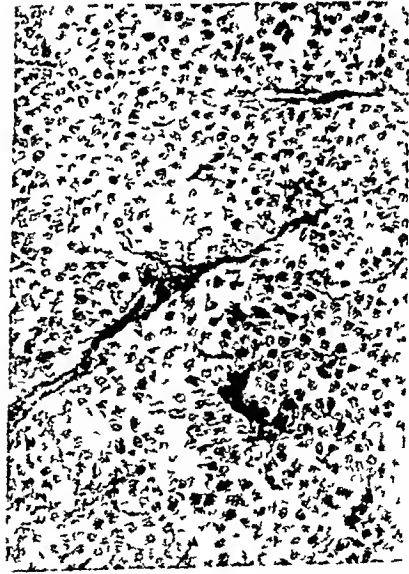
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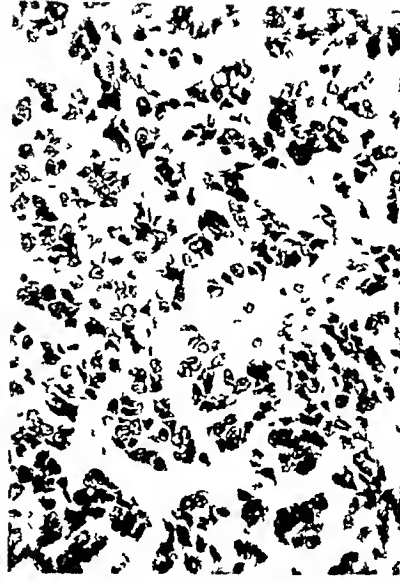
A2 Horizontal section of hypophysis showing adenoma on right of picture. The species mark the cleft. Eosin methyl blue. x66



B1 Horizontal section of hypophysis. Adenoma on right of anterior lobe tissue. Haematoxylin eosin. x66



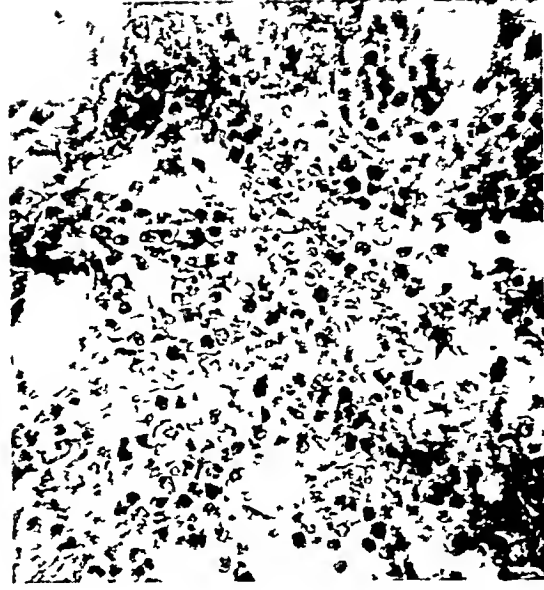
A3 A section of the same adenoma under high power. Eosin methyl blue. x400



B2 High power view of same adenoma. Haematoxylin eosin. x400



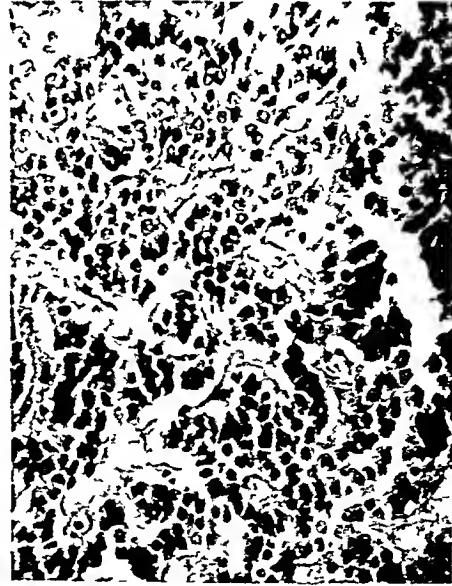
D1 Horizontal section of hypophysis Adenoma on right Eosin methyl blue x66



D2 High power view of same adenoma Eosin methyl blue x320



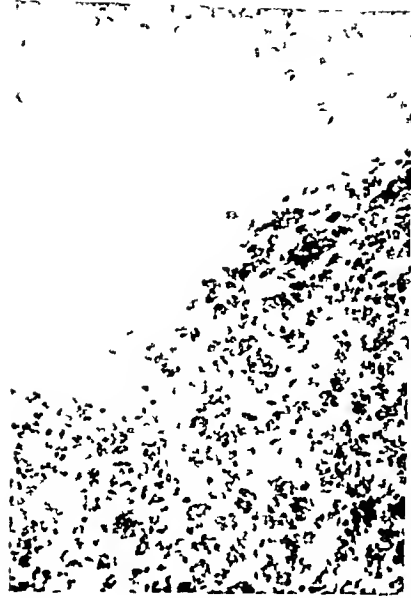
C1 Horizontal section of hypophysis Adenoma above Normal anterior lobe below Eosin methyl blue x66



C2 High power view of same adenoma Eosin methyl blue x320



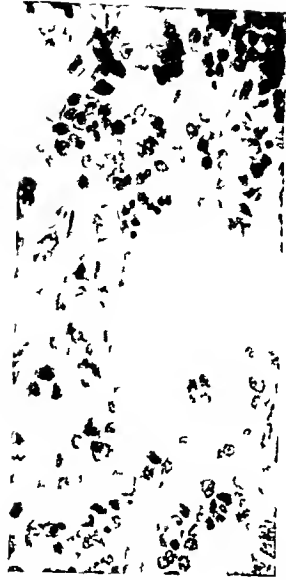
E1 Horizontal section of hypophysis Adenoma
above Normal anterior lobe below
Eosin methyl blue $\times 66$



E1 Horizontal section of hypophysis Adenoma
Eosin methyl blue $\times 66$



E2 High power view of same Adenoma
Eosin methyl blue $\times 340$



E2 High power view of same Adenoma
Eosin methyl blue $\times 340$

2 These adenomata were found accidentally on postmortem examination, and had not given rise to any clinical features

3 They are regarded as early tumour growths

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Obituary

Harold Beckwith Whitehouse

THE news of Beckwith Whitehouse's death on July 28th came with tragic suddenness to his many friends, and his early demise at the age of 60 leaves a blank in British gynaecology, and especially in Birmingham and the Midlands, which it will be difficult to fill.

Active to the end and still carrying his full load of work he collapsed as he was walking to the train after the meeting of the British Medical Association at which he had returned thanks for having been re-elected President, in a grateful little speech and apparently with his usual vigour. He was taken to University College Hospital where he rallied for a short time and even spoke of returning home by a later train, but a second and fatal attack followed and he died, as he would have wished, in harness. Mercifully for his family he had had a premonitory attack of angina, and so the blow, heavy though it was, was not altogether unexpected.

If he had been content to resign his appointments and to become a semi-invalid life might have been prolonged, but to a man of his activity, bubbling over with vitality and absorbed in his work, to be laid on the shelf while the tide of life rolled past could have presented few attractions.

Born in 1882 at Ocker Hill, Tipton, one of the Staffordshire iron towns, and only nine miles from Birmingham in which he was to spend his professional life, he went to Malvern College and then passed to St Thomas's Hospital for his medical training.

His student career was a brilliant one. He was entrance Science Scholar in 1901

and William Tate Scholar in 1902. In 1906 he graduated M.B., B.S., London, and was awarded the Sutton Sams Memorial Prize for work in obstetric medicine and diseases of women.

After qualifying he held posts as House Surgeon in a general surgical ward and in the obstetric and gynaecological department, and in 1908 took the M.S., London, with honours and qualified for the gold medal in surgery, and in the same year became a Fellow of the Royal College of Surgeons.

In 1908 he was appointed Honorary Assistant Obstetric Officer to the Birmingham General Hospital and so began his long connexion with this city which was to end only with his death. From the time of Lawson Tait, Birmingham has been one of the leading centres of obstetrics and gynaecology. Many famous names are associated with it and Whitehouse was soon to show that he was a worthy successor.

On the retirement of Prof. Thomas Wilson in 1921 he was promoted to the full staff of the General Hospital and at a later date carried this appointment to the New Queen Elizabeth Hospital, formed from the amalgamation of the General and Queen's Hospitals. He was also surgeon to the Maternity Hospital in Loveday Street.

For many years he was a member of the staff of the Birmingham University, first as assistant lecturer to Prof. Thomas Wilson, upon whose retirement in 1924 he was appointed to the combined chair of obstetrics and gynaecology. From the first he



HAROLD BECKWITH WHITEHOUSE

threw his great energy and personality into his clinical and teaching work, and soon acquired a wide reputation. What leisure he had in those early days was devoted to the study of pathology and research work.

Uterine haemorrhage was his first attraction and he contributed much to the elucidation of a complicated and difficult subject not yet completely solved.

In 1912 he was Hunterian Professor at the Royal College of Surgeons and lectured upon "The Physiology and Pathology of Uterine Haemorrhage."

In 1920, at the invitation of the Birmingham University, he gave the Ingleby Lectures, again on his favourite subject "Uterine Haemorrhage."

Uterine haemorrhage, however, was not the only subject which interested him and he wrote with knowledge and power upon many subjects connected with his branch of medicine.

His views were always sane and based upon sound premises and he soon built up a reputation as one of the leaders of British obstetrics and gynaecology. In 1935, when at the height of his professional activities, he found or made time to edit the fourth edition of Eden and Lockyer's well-known *Gynaecology*. In the light of recent knowledge many sections were completely rewritten and new ones were added. Only a man of amazing vitality and powers of concentration could have done this and done it so well amidst the heavy calls and distractions of his professional life at that period.

Perhaps as a clinician he was at his best. At the General Hospital, the new Queen Elizabeth Hospital and the Maternity Hospital, he had ample clinical experience and good use he made of it.

A cool, calm operator, he performed his task without fuss and flurry, getting the best out of his assistants and surprising onlookers, when they glanced at the clock

and found that these quiet proceedings had taken so short a time. Careful and methodical in diagnosis he had made up his mind beforehand what he intended to do, though when the unexpected was found he rapidly made a decision. It was a joy to watch a real master at work.

His patients, however, never became mere material upon which to exercise his skill. A naturally generous and sympathetic nature had been broadened and deepened by contact with suffering and every patient, hospital or private, received in full measure his sympathy and consideration.

In addition to his heavy commitments in Birmingham he was consultant to many hospitals in the surrounding area, the Lucy Baldwin Maternity Hospital, Hammerwich and Sutton Cottage Hospitals, the Smallwood Hospital, Redditch, the Guest Hospital, Dudley, Walsall and Nuneaton General Hospitals, and the Worcestershire County Council. He was never happier than when working at high pressure and he did much to improve the midwifery practice in this area. It was, however, performed at a great price, the expenditure of time and energy which had it been conserved might have avoided this tragic shortening of his career. It did, however, bring him into contact with large numbers of people, widened his knowledge and broadened his sympathies and made him, in a degree which falls to few medical men, one of the acknowledged leaders of his profession in his own area.

As was generally expected, when the British Medical Association decided to hold its annual meeting of 1940 in Birmingham, Whitehouse was selected by the local profession for the high office of President. Unfortunately the outbreak of war prevented this meeting from being held, but he was re-elected annually, as was Clifford Albutt in the last war, in the expectation

that when peace was declared he would preside and display to a wider circle his kindly hospitality and powers of organization

In 1930 the Congress of British Obstetrics and Gynaecology was held in Birmingham, over which he presided. This Congress was a great success, due largely to his careful organization and to his general supervision.

His teaching was clear, logical, and based on a sound foundation of physiological and clinical experience. Young men interested him and he was never happier nor showed better his qualities of heart and mind than when in their company.

From the earliest days of his staff appointment he not only entertained his house surgeon to dinner, but continued to invite him year after year until at last the company became too large for private entertainment and a club was formed. He told me himself of these annual dinners and how much he enjoyed them, meeting year after year young men whose early footsteps he had guided and whose career into middle life he had watched with affectionate care. To these men he was truly guide, philosopher and friend.

From his earliest days Whitehouse played a full part in public affairs and gave freely of his time and energy.

At first he was a regular attendant at the meetings of the obstetric and gynaecological section of the Royal Society of Medicine, of which he became a Vice-president, and of the Midland Obstetrical and Gynaecological Society over which he eventually presided.

Later, as his work and interests became concentrated more and more in the Midlands, he was not seen so often in London, though his old friends had hopes that when his term as President of the British Medical Association terminated we might persuade him to resume some of his old interests.

In 1914, within a fortnight of the outbreak of war, he was in France as officer in charge of the surgical division and surgical specialist to the No. 8 General Hospital, Rouen, and later of the No. 56 General Hospital, Etaples.

After this interlude he threw himself with redoubled zest into his own work. He was examiner in obstetrics and gynaecology at different times to the Royal College of Surgeons and the Universities of Sheffield, Bristol and Leeds, and also under the Central Midwives Board.

For four years he served as a member of the Radium Commission. He was well aware that radium is a double-edged weapon which may produce much harm unless used by skilled hands. He believed that in gynaecological cases it should be applied by a gynaecologist and in a pamphlet he set out the risks arising from its injudicious use.

An early if not original member of the Gynaecological Visiting Society, founded in 1911, he appears as a member in the minutes of the first meeting to be held in Birmingham in 1913. By a curious chance the last meeting of this society in 1938 was again held in Birmingham, when Whitehouse was the genial host and chairman.

At the meetings of this society, sometimes at home, sometimes abroad, in the company of a small group of contemporaries, all keenly interested in their work but enjoying in their leisure good comradeship, good entertainment, and good-natured banter, when stiffness and restraint are discarded and men reveal themselves in their true colours, Whitehouse was at his best. His appreciative chuckle at the good things provided or at a joke whether against himself or any other member, will long be held in affectionate remembrance. I can only recall one period of depression, when the hotel scales unexpectedly registered a gain of a stone. So deep was the

gloom that we had to confess that a friend standing behind him had added some pressure to the scales

In 1933 he visited the United States at the invitation of the American College of Surgeons and was made an Honorary Fellow of that college and also an honorary member of the Canadian Medical Society. When the first proposals were put forward in 1924 to found what is now the Royal College of Obstetricians and Gynaecologists he was an enthusiastic supporter. To provide a definite portal of training and examination for those who wish to practice this branch of medicine and to prevent, what at that time seemed possible, the separation of obstetrics from gynaecology, appealed strongly to him. In the five years during which we struggled for recognition he was of great service, and when the college was registered in 1929 he became a member of its first Council. Since he left the Council in 1937, and especially during the war period when his energies were more and more confined to his own region, the college unfortunately saw less of him. What made matters worse was his disregard of correspondence and the necessity of a long and costly telephone conversation if an early reply was required. In council he intervened only when he had a definite contribution to make and then stated his views firmly and clearly but generally ended with a little chuckle which removed any feeling of antagonism from those whose views he opposed. He was always listened to with respect and he wielded great influence.

In the birthday honours list of 1937 his name appeared as a Knight Bachelor, and it was hailed as a fitting recognition of the work he had done in the Midlands and of the position he had carved for himself in British obstetrics and gynaecology.

In 1909 he married Miss Madge Rae Griffith of Birmingham who with two sons,

one of whom is a member of our profession, and a married daughter is left to mourn him. Like so many successful men he owed much to a happy home life where he could relax and forget for a time the heavy burden he carried. Here he indulged, as much as his busy life would allow, his love of gardening, entomology and music. As a writer, clinician, and teacher, he had a great reputation, and it will be long ere his place is filled, and to those who knew him best his loss will be most felt. A staunch and loyal friend, always ready to give a helping hand to the young and those not so successful as himself, endowed with a clear brain and forceful personality which was ever at the command of any object which elicited his sympathy, and a boundless energy which was used unstintingly on whatever object he had in hand. A cheerful and hospitable nature which attracted many friends, he will be greatly missed.

To Lady Whitehouse and his family we extend our sincere sympathy in their great sorrow and to the Birmingham school in its great loss.

WILLIAM FLETCHER SHAW

As one who has received many kindnesses from Sir Beckwith Whitehouse over many years, and who has had intimate friends among his patients, I should like to add my tribute as a woman to the esteem and appreciation in which he was held.

He had a rare understanding of women in their strength and in their sufferings and I feel that we have not only lost a generous friend but one on whom we had learned to rely and to whom we could always look with confidence in our times of difficulty. He has left us, and carries with him the lasting gratitude of thousands of women in every walk of life.

Dear Becky! We thank you!

LUCY BALDWIN OF BEWDLEY

ALTHOUGH it is some 14 or 15 years since I last saw Beckwith Whitehouse, the announcement in *The Times* of his sudden death in London after presiding at a meeting of the British Medical Association came as a terrible shock to me, for despite the fact that we were unable to visit each other letters at Christmas kept the friendship alive. That friendship went back for more than a quarter of a century, to the days of Whitehouse's early married life when he did me the honour of asking me to be the godfather to his eldest child.

Looking back over that long period of years and trying to sum up in a few words the things which impressed me mostly in the character of my friend I am led to realize that he was one of the most generous and unselfish men I have ever met, his happiness consisted in using his vast energies in the service of other people, and this wonderful trait showed itself not only in large affairs but in all the small things of daily life, for example he did not play golf himself but, on occasion, he not only made a point of getting a match for his guest but followed the whole round himself as a compliment to his visitor. As co-examiners in the University of Birmingham, after our work was done he would always devise some special treat, such as a pre-arranged dinner at the "Lygon Arms," Broadway. This would be at the end of a hard day's work, involving a drive of some 40 miles into Gloucestershire. On the last of these occasions my wife and I were driven to his lovely country house, which was then in Shropshire, where he allowed his knowledge of horticulture full play, and I shall never forget the glorious display made by his beds of Iris.

It was always a regret to me that when he visited Plymouth in 1935 with Cuthbert Wallace and Russ for the Radium Commission he was unable to come on to Penzance to see my collection of flowering shrubs

and other botanical treasures dear to his heart, but although his letters lying before me at the moment speak of his desire and firm intention to see what the Cornish climate can do in the way of arboriculture that pleasure was denied to him.

A letter of his which I particularly value, because, though soiled thereby it otherwise escaped the conflagration when my cottage was burnt down, tells of his visit to Vienna and Budapest in 1935 with the G V S and of meeting some friends I had made when working with Wertheim in Vienna many years before. The man who impressed him most was Schiller. When our publishers wanted a fourth edition of Eden and Lockyer's *Gynaecology*, my colleague and I having both retired from practice, it seemed only natural to me that, with the approval of Eden, I should ask my friend Beckwith Whitehouse to undertake the task of editorship, his acceptance and the two years hard work he devoted to it greatly enhanced the value of our textbook.

The surprise and shock which his sudden death caused his friends and acquaintances was very terrible indeed within his family-circle, despite the fact that the life he had led since the outbreak of war was, to use his daughter's own expression, 'fantastic'. She says "he never came home till past eleven and was off again in the morning before eight, we never saw anything of him."

His passing-out laden with heavy toil and responsibilities is an impressive and memorable example of a true war-casualty, for in utter unselfishness he laid down his life for others.

CUTHBERT LOCKYER

IN Harry Whitehouse, as he was known by his friends, one of the most brilliant men of our day has been lost to us. I am unable to speak with authority of his eminence in his profession, though one of his most attractive characteristics was his willingness to talk of the scientific aspect of his calling to any humble learner in the fields of knowledge. What better could one ask for than that a man should talk of the things he understands? I often wonder why it is that those who know are so little apt to talk of the things they know, as those are the things one wishes to learn from them. Conversation is the medium through which we get to know our friends, and to talk with Harry Whitehouse was to gain an insight into a mind that was stored with limitless riches. Were I to look for the phrase that seemed best to convey the secret of his charm as a talker, I would probably find it to be the universality of his outlook. He was never the mere specialist. There was no field of science or art that he was not ready to explore with boundless enthusiasm. It was his breadth of outlook that gave weight to the expression of his views upon whatever the subject of talk might be. He had at the same time the true humility that distinguishes a fine mind. He was ever a learner and adding to his accumulation of intellectual gain and spiritual wealth.

He and Lady Whitehouse were the most charming of hosts, whether at Edgbaston or at their beautiful country seat in Monmouth. The warmth of their welcome, the generosity of their hospitality and the fine taste shown everywhere in their surroundings made a visit to their home an experience that lived in the memory. There was much too to delight the eye which might range from a fine piece of Jacobean furniture to a choice majolica dish of the Italian Renaissance. Nor was the art of to-day unrepresented as would appear from some splendid watercolours by one of the most

distinguished of our living painters. Their home was moreover an entomologists' paradise, the collection of British butterflies and moths being one of the finest that has ever been brought together. It was one exceptionally rich in rare species and outstanding varieties.

The pursuit of entomology was the recreation in which Beckwith Whitehouse delighted more than any other. Many a time have I watched with him round a collector's lamp until break of dawn. His excitement when an uncommon species was attracted to the light gave evidence of the spirit of youth that was always in him. A side of entomology that also particularly interested him was the scientific breeding of macro-lepidoptera, a sphere in which he was highly expert and obtained remarkable results. One of his achievements in this direction was the breeding of about a hundred specimens of the extremely rare and beautiful "Clifden Nonpareil" moth (*Catocala flavini*), a female of which he had the good fortune to capture. An account of his experiences in this process was published in *The Entomologist*. He was also the captor of an example of the "Alchymist" (*Catephua atchynusta*), as well as of several specimens of *Apamea zollnikofeni*, both insects of the utmost rarity in this country. He delighted in nature in all her manifestations, and his keenness as a gardener was hardly second to that as an entomologist.

Beside all this he was a man of the world, and the alertness of his mind and the charm of his manner made him at once an outstanding figure in whatever society he might find himself. Above all he was the kindest and most generous of men.

ARCHIBALD G. B. RUSSELL, M.V.O.,
LANCASTER HERALD OF ARMS

In spite of the eminent position Beckwith Whitehouse attained in his profession, he was seen at his best when at home with his family, when forming one of a shooting party or when engaged in entomology and gardening

It is impossible to imagine a more generous host, nothing was too good for his guests whose welcome was such that they might have been excused if they had fancied themselves one of the family

An original member of the Gynaecolo-

gical Visiting Society his presence at its meetings was always regarded with the most pleasurable anticipation, since he had that wonderful trait of making friends and retaining them no matter whether their respective opinions on many subjects were in agreement or otherwise

Most willing to assist any deserving object or person, the sum total of his great generosity will never be known His was indeed an unconquerable spirit

COMYNS BERKELEY

REPORTS ON HOSPITALS AND DEPARTMENTS OF PUBLIC HEALTH

THE NOWROSJEE WADIA MATERNITY HOSPITAL BOMBAY NINETEENTH ANNUAL REPORT FOR THE YEAR ENDING 1941

THE 19th annual report records that the number of births increased from 5 091 in 1940 to 5 813. This increase imposed a severe strain on the medical and nursing staff but that the work was efficiently carried out is undoubted, as is evident from the records. Details of the year's work are recorded in tabulated form, one notes the low forceps rate of 1.6 per cent and the high incidence of craniotomy namely 0.6 per cent. The mortality-rate of 20 per cent for eclampsia is high routine treatment was carried out in each case but details are not given of the method employed. Ninety one cases of placenta praevia are given all are stated to be postnatal which is a little confusing. There seems little advantage in working out the maternal mortality-rate as a percentage of the total admissions the figure still remains high but there is a general trend towards improvement. The number of deliveries is given as 5 644 in Table 25 which cannot be correlated with the figure 5 813 previously recorded. Anaemia accounted for 25 maternal deaths out of 89 this is an appalling figure and leaves much to be desired. It is difficult to appreciate the circumstances in which the work of this hospital is carried out but it is certain that the medical staff is keenly aware of a scope for improvement and doubtless is ever striving towards it.

THE ANNUAL REPORT OF THE ELSIE INGLIS MEMORIAL HOSPITAL

THIS brief report deals with the In-patients, which number 1 359, and the district cases which number 492. We note that 110 were admitted for antenatal treatment including several abnormalities which surely must have provided very admirable teaching material. The results of treatment appear to have been reasonably satisfactory. The maternal mortality-rate of 0.86 per 1 000 is a gratifying one. The notes on maternal morbidity are somewhat difficult to follow particularly the statement that included in one or other of these lists are 11 cases of septicaemia or local genital infection. A list is given of the

various abnormalities of pregnancy and labour results of which are within range of the usual average figures. An incidence of 60 cases of contracted pelvis seems to be on the high side particularly as a note is made that the contraction involved the pelvic outlet only in 14 cases. We are accustomed to teach that contraction of the pelvic outlet only without reduction in the size of the brim or cavity, is an extremely rare abnormality.

Under the heading Breech Delivery mention is not made as to whether external version was attempted and 3 patients delivered by Caesarean section are included in the statistics. Foetal mortality of 35.3 per cent for multiparous deliveries seems extremely high and the practice of induction for breech presentation is one of which we have but little experience. The forceps-rate exceeds 16 per cent which seems a little on the high side and the indications include 1 case of antepartum haemorrhage which surely in itself is not an indication for extraction by the forceps. Forty-four Caesarean sections were performed for non-paternity of the cervix a term with which we are not very familiar.

Postnatal complications included 72 cases of breast abscess which seems to indicate a need for a revision of the antenatal care of the breasts and a closer supervision of the patient during the period of lactation.

The bacteriological report is interesting and the example might well be followed by other maternity hospitals particularly the taking of a vaginal swab before surgical induction is undertaken. There is no mention of the type of haemolytic streptococcus encountered and the incidence of bacillus coli in the postnatal cultures (722 positive cultures) is interesting.

The report concludes with a paediatric section in which a summary of complications in the newborn is given and a short analysis of the stillbirths.

O LLOYD

ERRATA

In the August 1943 issue of the Journal under Reports on Hospitals page 304 the publishers regret that through a printer's oversight the word 'malaria' should have read *miliana*.

Review of Current Literature

- Director FREDERICK ROGUES M A M D M Chir (Cantab) F R C S, F R C O G

THIS Review contains the lists of contents and abstracts of the more important articles from the journals with which the *Journal of Obstetrics and Gynaecology of the British Empire* exchanges

The Review of Current Literature has kept the readers of the Journal in touch with current literature throughout the world owing to the war many

journals with which the *Journal of Obstetrics and Gynaecology* previously exchanged are no longer received. At the end of the year an Index of all the subjects contained in the articles of the journals reviewed is printed. Arrangements were made to include abstracts of important articles on borderline subjects such as Physiology, Biology and Biochemistry.

LIST OF ABSTRACTORS

J LYLE CAMERON, F R C S

W E CROWTHER M B

R H B. ADAMSON M D

B JEAFFRESO, F R C S

P MALPAS F R C S

T N A JEFFCOATE F R C S

MEAVE KENNY F R C S

JANE H FILSHILL

The British Medical Journal

November 7th 1942

*Clinical significance of the Rh factor (I) K E Boorman, B E Dodd and P L Mollison
Foetal and postnatal circulation (Leading article)

November 14th 1942

*Clinical significance of the Rh factor (II) K E Boorman, B E Dodd and P L Mollison

November 21st 1942

Spontaneous detachment of the cervix in labour
M D Westerman

December 5th 1942

*Infant and maternal mortality (Leading article)

CLINICAL SIGNIFICANCE OF THE RH FACTOR

Human erythrocytes contain A and B agglutinogens of Landsteiner and a variety of antigens the best known being the M and N

The corresponding antibodies to M and N occur only rarely in human sera and these factors although acting as antigens when injected into certain animals rarely stimulate the production of immune antibodies in man

The Rh factor owes its importance to its ability to stimulate the function of specific immune agglutinins in man

Rhesus monkey blood is injected into rabbits. The resulting serum when tested with human blood shows that 85 per cent of bloods are agglutinated whilst 15 per cent show no agglutination. The former are termed Rh positive. Persons who are Rh-negative are capable of forming an antibody which reacts with the Rh antigen. This may occur after transfusions of Rh positive blood or more commonly when an Rh negative woman becomes pregnant and the foetus is Rh positive.

It was found that whereas only 15 per cent of the random population were Rh negative 92 per cent of mothers who had given birth to infants affected with erythroblastosis foetalis were Rh negative. Examination of the husbands and children in this group showed that all who were tested were Rh positive. It was also maintained that infants affected with erythroblastosis foetalis remained less anaemic after transfusion with Rh negative blood than with Rh positive blood.

The heredity of the Rh factor was considered by Landsteiner and Wiener. They suggested that two allelomorphic genes, Rh and rh, were concerned the Rh being dominant. When the husband's phenotype is Rh positive and that of the wife Rh negative the phenotype of the baby will

depend upon whether the husband's genotype is RhRh or Rhrh. If the former, the infant's genotype will be always Rhrh and the phenotype therefore Rh-positive. If the latter the phenotype will be Rh-positive only in 50 per cent of the siblings.

Test serum may be obtained from an animal which has been immunised by a course of injections of blood from rhesus monkeys or from a human individual who has become immunised to the Rh antigen. The disadvantage of animal serum is that only small quantities are obtained and it also contains other antibodies which have to be absorbed capable of acting on human erythrocytes.

The article describes the technique of the tests and then goes on to the results. Of 48 mothers who had infants with undoubted erythroblastosis 46 were found to be Rh negative and in 44 cases Rh antibodies were present. In all 48 cases the infant was Rh-positive.

The suggestion is made that certain cases of so-called physiological jaundice are really mild-erythroblastosis. Repeated transfusions of Rh-positive blood to an Rh-negative individual may be followed by a haemolytic reaction due to the production of Rh antibodies from the earlier transfusions.

Women who have given birth to an infant suffering from erythroblastosis are very prone to severe intra group haemolytic transfusion reactions.

For the transfusion of recently delivered women it is desirable to have a panel of Rh-negative donors available. As routine transfusions on a large scale with Rh negative donors will be impracticable the donor's cells should be tested against the recipient's serum. The most suitable person for an affected infant will be a Group O Rh-negative person.

INFANT AND MATERNAL MORTALITY

This article reviews the report from the Department of Physiology of Durham University which considers infant mortality from the sociological viewpoint.

It has been found that the lowest infant death rates are found in first, second and third children born to mothers between 20 and 35 and fourth and fifth children to mothers between 35 and 40. The infant death rate is abnormally high among first children born to mothers under 20 and over 30.

It is evident that the age of a mother at the birth of her first child and the spacing of the family are matters of prime importance. The same conclusions hold good when maternal mortality is considered. The death-rate of primiparae over 30 years is four times that of primiparae between 20 and 35. The facts explain the absence of improvement in maternal mortality-rates in the more favoured classes where late marriage is the rule.

JOHN HAMILTON

The Canadian Medical Association Journal

Vol XLII, July 1942 No 1

- *Sex hormones in obstetrics and gynaecology
Max M. Cantor, J. R. Vant, the late L. C. Conn and M. J. Huston
- *Duplication of the uterus and vagina
Gordon E. Perngard
- *The influence of menstruation on carbohydrate tolerance in diabetes mellitus
H. I. Cramer

SEX HORMONES IN OBSTETRICS AND GYNAECOLOGY

This paper is an exposition of the effects of the sex hormones and a comparison of their activities so far as is known and the reported experience of the use of these hormones in certain disorders. The oestrogenic phase or proliferative part of the cycle is induced by oestrogenic hormones; the contractile power of the uterus is induced, and

secretion from the thickened endometrium is also brought about. Ovulation occurs about the mid-interval of the cycle and is followed by the conversion of the follicle into the corpus luteum, which in turn secretes progesterone which causes conversion of the proliferated endometrium into the functional secretory type thereby preparing the endometrium for the nidation of the fertilized ovum now travelling towards the uterus. Furthermore progesterone counteracts oestrogen and causes relaxation of the myometrium. It also stimulates development of the acini of the mammary glands. The vaginal mucosa also shows proliferative development.

When pregnancy occurs the corpus luteum survives its course is prolonged causing development of a decidua. If fertilization does not occur

the corpus luteum degenerates, and in consequence the highly specialised endometrium disintegrates and is shed resulting in menstruation. The mammary glands also undergo involution.

When pregnancy has occurred, about the end of the third lunar month twelve weeks the placenta assumes the function of an endocrine gland and secretes large amounts of an endocrine one which, in turn, stabilises pregnancy.

Pituitary gonadotropins stimulate ovarian and testicular activity in hypophysectomized animals. There is no evidence of their value when applied to human beings. Gonadotropins obtained from the serum of pregnant mares contain follicle stimulating factors. Their clinical value has not been proved.

Gonadotropins from the urine of pregnant mares are products of the chorionic cells. They appear in the urine during intra-uterine and extra-uterine pregnancy, in hydatidiform mole, chorion-epithelioma and carcinoma testis. They have a more powerful effect in stimulating development of the corpus luteum and therefore tend to suppress menstruation. Their use clinically is not of great value. They are inactive when given orally.

Prolactin has little clinical value at present.

Several oestrogens such as oestrone, oestrinol and oestradiol are valuable. Their actions are identical but the intensity and duration of their action vary. Progesterone cannot effect its characteristic endometrial response without preliminary stimulation by oestrogen and similarly prolactin cannot produce lactation without preliminary stimulation of the acini ducts and mammary glands by a sufficient amount of oestrogen and progesterone in this order. Oestrogens stimulate the growth of the epithelium of the vagina causing thickening and hyperaemia and have been extensively used in vulvo-vaginitis, kraurosis, leukoplakia and genital hypoplasia associated with amenorrhoea, sterility and menopausal degeneration.

Progesterone is the most common example of the group of progestogens. It is useful in functional uterine bleeding in threatened abortion, habitual abortion and in some cases of premature labour. When a functioning endometrium is present progesterone brings about the change from oestradiol and oestrone to the inactive excretory form oestrinol.

Androgens, contrary to common belief, do not neutralize the effect of oestrogen but rather exert a co-operative action. It modifies the action of oestradiol and increases the secretion of oestrinol thereby inhibiting intermittent uterine contraction of the spiral arterioles and thus diminishes the blood flow to the endometrium. In this way it is useful in the treatment of uterine bleeding due to any cause, and it relieves dysmenorrhoea and some forms of mastodynia.

Gonadotropins must be freshly prepared. They generate rapidly and must be administered by injection. Preparations from serum are follicle stimulating; those from pregnancy urine are luteum stimulating.

Progestogens when prepared from the corpus luteum, are less active than progesterone which is again four times as active as the oral preparation pregnenolone.

Androgens of which testosterone propionate is the most active known when measured by its effect on the seminal vesicles, is seven times as potent as testosterone and its effect is doubly prolonged. It may be given by mouth effectively and has a methyl derivative.

Oestrogens. Oestrone is a poor and ineffective preparation. Oestradiol is the form in which the hormone exists in the ovary. It may be given orally, intramuscularly, by injection or in a vaginal suppository. Oestrinol is an excretory product of oestradiol. It is active orally, but inactive intramuscularly. Oestradiol benzoate or dipropionate is freely soluble in oil and its action is intense and prolonged. It is best administered by intramuscular injection or by injection. It is useful when required for prolonged administration. From experiments it would appear that oestradiol dipropionate is the most economical and effective oestrogen known at present, providing effective treatment with little inconvenience to the patient.

The authors have used sex steroids by two routes: first, by subcutaneous implantation of pellets and second by employing a solution of the material in propylene glycol which is administered with a dropper under the tongue from this region the steroids are rapidly absorbed. This method is practical and economical.

CLINICAL CONSIDERATIONS

One of the chief uses of the pregnancy test, to determine the presence of chorionic gonadotropins

is in the diagnosis of chorion epithelioma and its recurrence. The value of the test for the diagnosis of pregnancy is of course, well known. Progesterone is not found in the urine as such as it is excreted as pregnandiol, which however, occurs in the urine in too small quantities to be determined satisfactorily. It is of value in cases of basophilism to differentiate between the pituitary and adrenal types.

The activities of the ovaries can be determined by two simple methods, the first is examination of a small fragment of endometrium sucked from the uterus, the second is simpler and consists of the study of a vaginal smear.

Disorders of the menarche These disorders may have an organic, nervous, or endocrine basis. Emotional disturbances, changes of environment, faulty nutrition and hypothyroidosis all have an effect on menstruation. Hypoplasia of the ovary may result from weak pituitary stimulus or weak ovarian response. The result would be inadequate secretion of oestradiol and consequent uterine hypoplasia. Occasionally the uterus fails to react to normal ovarian secretion and the menstrual flow is scanty or absent or the interval between the periods is greatly lengthened. In some cases ovulation may fail to occur. The follicles develop into cysts with excessive production of oestradiol, the corpus luteum fails to form and to elaborate progesterone, with resulting menstrual irregularities such as profuse bleeding or mild prolonged haemorrhage.

Amenorrhoea and oligomenorrhoea The first effort should be directed to promoting development of the uterus to normal size by administering large doses of oestrogen supplemented by progesterone during the second half of the cycle. The authors routine is to administer thyroid extract to the limit of tolerance without regarding the initial basal metabolic rate unless this is increased beyond plus 20. Oestradiol dipropionate (di ovocyn) is given every four days throughout the cycle, and progesterone (lutocyn) is given on the seventeenth, twenty-first and twenty-fifth days. This is usually followed by menstrual bleeding and this procedure is repeated until two or three periods have been produced. In the majority of cases of secondary amenorrhoea menstruation is regular after such treatment if there is a relapse this routine is repeated. Oligomenorrhoea and hypo-

menorrhoea are more responsive to this treatment than amenorrhoea, the primary type being rather resistant. When the patient is in good health and there is no especial desire for pregnancy, there is no indication, beyond the giving of thyroid extract and a suitable diet to press such treatment. When there is definite uterine hypoplasia resulting from defective ovarian secretion, the treatment is usually unsatisfactory. On a theoretical basis the follicle stimulating hormone should be given for the first fortnight of the cycle, and the luteinizing hormone for the last two weeks. Such treatment is usually disappointing, occasionally ovulation may be produced by the intravenous administration of 40 to 80 Ru of mare's serum gonadotropins. There is however, considerable risk of anaphylactic shock or serum sickness. Small doses of deep X-rays to the ovaries may be beneficial to render the ovaries inactive in the hope that when they again function this may be exaggerated up to what should be normal level.

Menorrhagia metrorrhagia, metropathia haemorrhagica Functional irregularities in uterine haemorrhage are due to imbalanced productive action of the ovaries upon the uterus. The cause of the haemorrhage comes from the excessively hypertrophied endometrium and is not well understood, the usual theories advanced will not be discussed here. Gonadotropins have been given in excessive doses in the hope of stimulating development of the corpora lutea, but this may produce the opposite effect by promoting an excessive oestrogenic secretion, already over-abundant. The authors have found two procedures to be of value, the first is the use of progesterone which counteracts excessive oestrogen elaboration and transforms the hyperproliferated endometrium into a secretory form. Four intramuscular injections of 5 to 10 mgm are given every second day after the twentieth day of the cycle. In mild cases 2 mgm may suffice, in more severe cases the injections may be supplemented with pregnenolone, 5 mgm daily by mouth. When such measures fail testosterone propionate 10 to 25 mgm once or twice daily for two consecutive days, should be given, the first dose on the second or third day of the haemorrhage. Usually there is a response within 12 to 24 hours. Additional treatment with methyl-testosterone orally in the second half of the interval has been found useful in preventing

recurrences The authors are of the opinion that testosterone propionate is a powerful remedy against uterine bleeding Occasionally a sharp haemorrhage lasting about 15 minutes starts 12 to 24 hours after the administration of testosterone but if the patient is warned, anxiety is avoided

Dysmenorrhoea The cause is obscure but many investigators believe that it is due in some way to increased myometrial activity associated with hyperoestrinism Androgens are the most effective remedy Testosterone propionate, 5 to 10 mgm according to the intensity of the symptoms is injected on alternate days the first dose to be given just before the symptoms are due and the treatment carried on throughout the time of the pain The subsequent period may be scanty or absent, and several successive periods may be affected but eventually a cure is effected The danger of producing hirsutism has been suggested but the authors have given up to 300 mgm per month for three months without any suggestion of masculinization The minimal dose to produce such an effect would be about 500 mgm a month and this is far beyond the demands of therapeutic necessity

Menopausal syndrome It is believed that the clinical symptoms are proportionate to the intensity of the degree of oestrogen deficiency When menorrhagia is not a prominent symptom the authors give oestrogens intramuscularly employing oestradiol dipropionate (di ovoclyn) when symptoms are severe, 5 mgm are injected weekly for three or four weeks, then 1 to 2 mgm are given weekly or at intervals of 10 days When symptoms are mild they may be controlled by an injection of 1 mgm every 14 to 21 days The treatment is continued until the interval between injections can be as long as a month without a return of the symptoms The patient's estimate of her symptoms is a poor guide fragments or vaginal smears are of much greater informative value The vaginal epithelial cells change from a round or oval shape to large squamous cells in 4 to 6 days after the first injection Some patients are highly resistant to treatment with oestrogen, the use of which should be discontinued if there is no improvement within 2 or 3 weeks When this is the case and especially when menorrhagia is present testosterone propionate in doses of 10 to 25 mgm weekly is given until the symptoms are controlled

The dose is then decreased and the interval lengthened

Vulvo vaginitis This is difficult to treat when there is infection of an immature vagina In the newborn child the mucosa of the vagina under the influence of maternal oestrogens is thick the secretions are acid and the flora of bacillary type Within a month following birth the vaginal mucosa becomes thin and the secretions alkaline and scanty it remains in this vulnerable state until puberty when oestrogens again convert it into the thickened form After the menopause the mucosa again becomes thin and atrophied as in the prepubertal state and it becomes liable to infection and trauma Vulvo vaginitis is treated with oestradiol dipropionate (di ovoclyn) 2 mgm every four days for six doses are given then at weekly or ten day intervals for another 4 to 6 weeks This promotes epithelization of the mucosa and produces acid secretions The treatment is augmented by vaginal suppositories containing 0.4 mgm every night for a week or ten days continuing on alternate nights until a clinical and bacterial cure is reached If the cure is complete there should be no recurrence at the end of a month Recurrences after three months are invariably due to reinfection

Senile vaginitis pruritus vulvae and kraurosis Smears taken from the vagina show extreme oestrogen deficiency The authors treat this case with di-ovoclyn 2 to 5 mgm at weekly intervals together with 0.4 mgm in suppositories on alternate nights for four weeks This increases the thickness of the epithelium This state may be maintained by vaginal suppositories of reduced dosage twice weekly Regression should be treated with further intramuscular injections Pruritus vulvae and leukoplakic vulvitis arising 10 to 15 years after the menopause and kraurosis require intensive treatment The treatment outlined for senile vaginitis is supplemented by a local application of 1 mgm of oestradiol propionate in 1 gram of adeps lanae for three or four months and the course repeated after four to six months

Cystic disease of the breast The lobular type is a painful hyperplasia of the terminal ducts and acini of the breasts associated with the formation of small cysts It is usually associated with hyperactivity of the ovaries and pituitary gland Oestradiol dipropionate and progesterone or

oestrogens alone may be given in the mid interval of the menstrual cycle. Symptoms tend to recur after three or four months and the treatment must be repeated. Cystic hyperplasia (mastodynia) is the type more commonly known and is associated with cystic ovarian disease and over production of oestrogens. Circumscribed cysts develop in the centre of the breast due to continuous proliferation. Relief from symptoms can usually be obtained completely and without recurrence by the administration of testosterone propionate, 25 mgm once or twice daily for two or three days. This acts by completely depressing oestrogenic activity. The menstrual period succeeding this treatment is scanty, delayed or absent. Testosterone propionate is also employed by the authors with excellent results in cases of gynaecomastia associated with adolescence. A weekly injection of 25 mgm is given for two or three months. This allays pain and reduces the size of the breasts.

Threatened abortion, habitual abortion and premature labour. Progesterone—elaborated by the placenta—inhibits the excretion of pregnandiol which, again, is liable to precipitate the above-mentioned accidents. The dosage must be very large to be effective: normally 20 mgm are excreted every day until the third month of pregnancy and this amount must of necessity be replaced.

Five very full tables containing classification, nomenclature, standardization, excretion and synopsis, effects, tendencies and treatment, together with a plate containing numerous highly illustrative drawings, are included in the text.

DUPLICATION OF THE UTERUS AND VAGINA

A case is reported of a primigravida three months pregnant in whom two distinct vaginae were discovered, two cervixes and as far as could be ascertained two uteri: this is an unusual developmental condition ordinarily seen in monotremes and some of the lower marsupials. The condition is due to the non fusion of the lower ends of the Mullerian ducts. In this patient the vaginal septum was well formed, vascular and thick. Pregnancy was established in the left uterus. The vaginal septum was removed and the pregnancy maintained without mishap.

The text includes a fairly full discussion of anomalous developments of the uterus with all degrees of non fusion of the lower ends of the

Mullerian ducts, involving double uteri and double vaginae in all degrees. Various abnormalities of menstruation, pregnancy and parturition are briefly outlined.

The text includes two drawings of double vaginae and a series of exceptionally clear diagrams. A short bibliography is appended.

THE INFLUENCE OF MENSTRUATION ON CARBOHYDRATE TOLERANCE IN DIABETES MELLITUS

Diabetes mellitus has long been known to exert a pronounced influence on menstruation and on sexual functions. Amenorrhoea was quite commonly associated with impairment of libido and with sterility. Similarly the male may be affected with impotence and sterility. Quite frequently the uterus and ovaries atrophy in diabetic patients. All of these conditions, however, have more or less disappeared or have been kept under control since the introduction of insulin treatment.

It was demonstrated by animal experiments in an animal rendered absolutely diabetic by pancreatectomy, that the diabetic state was greatly relieved by hypophysectomy, while conversely the administration of anterior pituitary extract aggravated the diabetic condition. Even in the animal with normal pancreas free administration of anterior pituitary extract produced diabetes. Sometimes the diabetic condition persists after cessation of the administration of anterior pituitary substances. This has been shown by the work of numerous investigators. The author has made extensive investigations into the relations existing between menstruation and carbohydrate tolerance in diabetic patients. The results of these investigations have led to some interesting conclusions. It has been shown that there is a definite impairment of carbohydrate tolerance in some diabetic patients at the menstrual period. This impairment may be so severe as to precipitate diabetic acidosis and coma. However this disturbance in carbohydrate metabolism may not occur in all diabetic women at the time of menstruation nor may it occur to anything like the same extent at every menstrual period in the same patient. In comparison with this it has been shown that there is a much smaller incidence of diabetic acidosis in males than in females below the age of 45 years, although during this period diabetes is much more common in males than in

females This more frequent occurrence of acidosis in females appears to be associated with those occurrences of acidosis at the time of the menstrual period

Two illustrative tables, and one figure are included in the text, and a very full bibliography is appended

J LALE CAMERON

Medical Journal of Australia

June 20th, 1942

*Intestinal obstruction at the seventh month of pregnancy, due to long standing and extensive peritoneal adhesions of obscure origin P L Hipsley

June 27th 1942

Pregnancy in the syphilitic mother Current comment

July 4th 1942

Carcinoma of the uterine fundus Current comment

INTESTINAL OBSTRUCTION AT THE SEVENTH MONTH OF PREGNANCY

Hipsley describes the case of a primigravida aged 25 years who was referred to him with the diagnosis of acute hydramnios

There was a history of increasing constipation from the end of the seventh month of pregnancy and, within a few days, an acute intestinal obstruction

On opening the abdomen adherent coils of small bowel had to be separated from each other, and from the anterior uterine wall As the enormous intestinal distention and the uterine enlargement both rendered it impossible to explore the abdomen it was decided to reduce the size of the uterus by Caesarean section and then to carry out a thorough

examination of the intestine which had to be entirely eviscerated

After the uterus had been emptied it was found that the small and large bowels were adherent to each other throughout their length The adhesion could be separated after dealing with each coil piecemeal, and there was no kinking of any portion of the bowel but rather a general distension of the gut throughout its length At one point two loops of small intestine had become adherent with a fistulous opening between the two just as though a lateral surgical anastomosis had been carried out

After the whole length of the bowel had been freed with the exception of the anastomosis an appendicostomy was made and the gut returned to the abdomen

The patient made a good recovery with some post-operative ileus The patient was a twin the other child being stillborn After birth she was very ill for several weeks and was not expected to survive

The writer's suggested explanation of the origin of the condition was that the patient had suffered from general peritonitis in infancy, and that the lateral anastomosis had occurred at this time and had probably saved her life The extensive adhesions prevented any localized kink which might have given rise to an earlier acute intestinal obstruction

R H B ADAMSON

American Journal of Obstetrics and Gynecology

Vol 41 No 4

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Conglutination of fibrin ex utero as a factor in delayed labour P J Carter

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- A study of 107 cases of uterine bleeding with endometrial biopsies G F Douglas
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- *Pituitary shock M H Adelman and B B Lennon
- Cancer of the cervix following supravaginal hysterectomy G Gray Ward
- Some clinical observations on the endocrinology of abortion E C Hamblen
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- *A clinical study of progesterone therapy by pellet implantation D R Mishell
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INHIBITION OF LACTATION

That the degree of early breast engorgement does not consistently indicate the amount of subsequent milk production is the experience of most obstetricians and has been verified by the authors of this paper during a study of normal lactation

among 900 consecutive nursing mothers. This fact must be borne in mind when assessing the therapeutic value of stilboestrol, testosterone and theelin which have been used to decrease engorgement and have been reputed to inhibit lactation. The authors decided to investigate whether inhibition of breast engorgement was synonymous with inhibition of lactation and whether these substances would inhibit breast secretion after lactation is established and whether the effect was temporary or permanent.

Stilboestrol was administered to 29 nursing mothers beginning with the first post-partum day. Of these 23 had a good nursing history and six had a poor one. Six mothers with good histories who received 15 mgm to 35 mgm of this substance secreted sufficient milk on the fifth and twelfth days for full nursing from the breast. Six similar mothers who received 15 mgm to 50 mgm were limited to part-time feeding by the fifth day but all increased to full-time nursing by the tenth day. There was no engorgement during the first few days in either group. In 11 cases there was a deficiency of lactation on the fifth day but eight of these were on full breast by the tenth day, two increased to part-time nursing and one was taken off the breast entirely. Of the six mothers with a poor nursing history, who received a similar dose of this drug all remained deficient on the fifth day and only one increased to part-time nursing by the tenth day. In no case were they able to inhibit lactation once it had been established though three out of 23 good nursing mothers were reduced to part-time feeding by the tenth day. They came to the conclusion that in spite of larger doses once lactation was established the effect of stilboestrol was much less than when it was given before lactation was in full swing.

With testosterone given in doses of 125 mgm only two out of 15 good nursing mothers were reduced to part-time feeding on the fifth day and one of these was on full nursing by the tenth day. In no case was a deficiency of lactation established and no change at all was noted when this drug was given after full lactation had been established.

Theelin was given to 10 patients five in the early post-partum and five in the late post-partum period. Each received 250 000 international units of the drug. The incidence of full breast feeding was not affected and as in the

testosterone series the breasts were full but not engorged. With these data the authors came to the conclusion that the inhibition of breast engorgement was not synonymous with inhibition of lactation. Also, that engorgement of the breasts can be prevented by suitable doses of stilboestrol, theelin or testosterone and that the stilboestrol can cause in some cases a temporary decrease in the amount of lactation.

CONGLUTINATIO ORIFICII EXTERNI AS A FACTOR IN DELAYED LABOUR

Only a few cases of this condition have been reported in the literature but Carter is of opinion that it is not as infrequent as is generally supposed. He describes the anatomy of the cervix and stresses the importance of the preponderance of circular muscle bundles in this part of the uterus. Failure of dilatation of the circular fibres around the external os with adequate dilatation of the circular fibres of the remainder of the cervical canal, constitutes the primary lesion of this condition. He mentions five or six possible causes including scarring following operation upon or syphilitic infection of the cervix. He also says that it can occur in either primigravidae or multiparae but that it did not tend to recur in subsequent pregnancies. Clinically, it is recognized late in labour by finding the whole cervix thinned out over the advancing head or bag of waters causing dystocia. The external os is difficult to locate and may be felt only as a tiny pin point depression where the os would normally be located. On speculum examination it is sometimes impossible to identify the situation of the os but in most cases a tiny hole can be seen surrounded by a very red ring. If the condition is not recognized the cervix is likely to become oedematous from disturbance of the circulation.

Carter reports three cases of his own experience and recommends continued gentle and steady digital pressure upon the depression which represents the external os. This is usually successful further dilatation occurs at once and delivery quickly follows. Although manual or instrumental dilatation may be necessary in some cases Carter does not recommend it because of the risk of uncontrolled tears developing. He advises controlled incisions into the cervical tissue if the dilatation is delayed after the digital pressure.

He states that in his opinion the term conglutination is a misnomer as the condition is due to a failure of dilatation of the circular fibres round the external cervical os.

PITUITRIN SHOCK

Untoward reactions occasionally follow the use of pituitrin and it is necessary with so valuable a therapeutic agent to consider their cause in every case. With pituitrin the chief reaction is that of shock but cases have been reported in which pruritus and angio neurotic oedema have occurred with or without the shock. Such cases imply that some patients are sensitive to the extract, especially if there is a history of some previous injection and that an anaphylactic basis must be ascribed to explain such phenomena. Besides this explanation the theories of histamine reaction and effects on the heart have been advanced in the literature on this subject.

The authors report seven cases which are specially interesting and unique as the reaction occurred while the patients were under the influence of surgical anaesthesia. Six of these cases occurred in women on whom vaginal hysterectomy was being performed and who received, early in the operation 1 to 2 c.c. of pituitrin to decrease the amount of bleeding in the operation field by local vaso-constriction. The other case occurred during Caesarean section. Two of these seven cases are reported in detail and in all of them the picture of shock supervened a few minutes after the injection, with a rapid pulse rate and a marked fall of blood pressure. The absence of significant haemorrhage and surgical shock in the cases of vaginal hysterectomy and the prompt appearance of shock after the administration of the pituitrin, point unequivocally to the pituitrin as the responsible agent.

The authors are of the opinion that in their cases the theory that the shock was a histamine reaction was out of the question as the solution used was histamine free. They think that many of the cases reported in the literature, especially those that develop oedema were examples of the phenomena of anaphylaxis but that their cases were examples of the cardiovascular effects of pituitrin. They maintain that the view commonly held that the injection of a posterior pituitary extract results in a rise of arterial pressure is

erroneous It is generally agreed that the experimental pressor response to pituitrin is due to arteriolar and capillary constriction and therefore some other explanation must be found for the fall of pressure in cases of pituitrin shock They report that one worker showed that the pitressin fraction possesses a potent constrictor effect upon the coronary arteries this effect leads to anaemia of the myocardium, which varies very much in degree and finally to dilatation of the heart This has been demonstrated by Roentgenography They are of the opinion that the cause of the shock in their cases was this cardiac effect leading to a decrease of cardiac output and a fall in pressure

During a discussion on treatment they recommend the administration of intra-venous fluids oxygen and adrenalin If it occurs during anaesthesia they do not advise the giving of adrenalin as it might cause nodal tachycardia which is an undesirable burden in an already anovaemic heart They do not think it wise to use pituitrin just to diminish bleeding at the time of operation and they warn us against injecting it directly into the uterine muscle at Caesarean section because of the risk of its being injected directly into a blood sinus They also think that every obstetrician should be prepared to meet cases of sensitivity to the drug especially when there is a strong possibility of a previous injection having been made

A CLINICAL STUDY OF PROGESTERONE THERAPY BY PELLET IMPLANTATION

Whenever progesterone is indicated for treatment it is usually necessary to administer it for long periods of time to get its full effect This entails a large number of injections of small doses

at frequent intervals and this is a great objection to many patients When a steady prolonged progesterone effect is desired the author advises the implantation of a pellet of the drug under the skin He has had most gratifying results with implantation of pellets of oestrone in the treatment of the menopause

In a group of cases of habitual or threatened abortion, dysmenorrhoea and functional bleeding he has implanted 45 to 60 mgm under the skin with local anaesthesia in the region of the left groin After incising the skin a channel of 2 cm length was made, at the bottom of which the pellet was inserted If the pellet was expelled spontaneously reimplantation was performed

The four cases of habitual or threatened abortion thus treated were most successful being either delivered of a full-time child or getting near to term at the time of writing this paper Of the six cases of dysmenorrhoea four gave satisfactory results These cases were observed for three to six months during which time the menstrual periods were almost entirely free of pain Of the functional bleeding group, 50 per cent of cures were obtained In the successful cases the endometrium showed a change from a persistent proliferative to a well-developed secretory phase They maintain that curettage must be performed in all cases of this group for evidence of progesterone lack In one unsuccessful case a preliminary study of the endometrium showed no evidence of either oestrone or progesterone activity This case might have responded to progesterone if the endometrium had been previously primed by oestrone therapy

BRYAN JEAFFRESON

The Journal of the American Medical Association

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- *The assay of gonadotropins and gonadot hormones
R Gustavson and F d Amour

Vol cxvii No 12, September 20th 1941

- *Results of radium treatment of cancer of the uterine fundus with special reference to the microscopic grade of the lesion R E Fricke and C O Heilmann

- *The electrolyte therapy of premenstrual distress
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- *The synthetic oestrogen diethylstilboestrol C MacBride D Castrodale L Loeffel and H Freedman

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*Treatment of the menopause evaluation of oestrogen implantation V Salmon, S Geist and R Walter

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*Spontaneous pneumo mediastinum in the newborn B Gumbiner and M Cutler

THE ASSAY OF GONADOTROPINS AND GONADOL HORMONES

The gonadotropic preparations which are used in clinical practice are derived from three sources the serum of pregnant mares, the urine of pregnant women and the anterior lobe of the pituitary. There are no chemical methods of assay available and only biological measurements can be used. Two of these biological tests the increase in weight of the seminal vesicles and the increase in weight of the ovaries after administration of the hormone are tests that can be carried out quite satisfactorily, but both possess one very real disadvantage namely a high individual variation rate. The difference in response observed in similar ovaries to a given dose of the hormone may be as much as 100 per cent and the same applies to the seminal vesical test.

Measurement of the increase in weight of the uterus is a good objective test and the great absolute weight of the uterus makes exact weighing less important. This test is very sensitive a six-fold increase in weight of the uterus being obtained with doses which will only double the weight of the seminal vesicles and hardly affect the ovarian weight. The main objection to the test is the high individual variation. This may be as much as 300 to 400 per cent and entails the use of large numbers of experimental animals.

The vaginal cornification test is perhaps the simplest and most satisfactory of all the biological methods of assay for the gonadotropins. Provided that the standard of a full oestrus smear is observed it is a reasonably objective test with a sensitivity quite equal to that of the uterine weight method. The lutemization method of assay is unsatisfactory in every respect.

International units have been established for the gonadotropins from the urine of pregnant women and from the serum of pregnant mares but none as yet for the gonadotropins derived from the anterior pituitary. The use of international units

has very great advantages but when working with them it is important to remember that slight differences in technique may lead to greatly varying results. Very close adherence to the details of any published technique is necessary if comparable results are to be obtained.

The second half of the paper reviews the biological and chemical methods of assay of the oestrogenic hormones as distinct from the gonadotropins. Chemical methods of assay are available and are being developed intensively in view of the difficulties inherent in the biological methods. Whatever biological method is used, the growth of the uterus of the immature rat or mouse, the growth of the uterus of the castrate rat or mouse or the vaginal smear method the response varies with many factors unconnected with the amount of oestrin used such as the route of application the frequency of dosage and the presence of non oestrogens in the extract injected. It is known that some of these non oestrogenic impurities accentuate the activity of the oestrogens.

The chemical methods of assay can be divided into two main groups spectroscopic and colorimetric. The authors give a list of the various methods which have been used. In the case of the corpus luteum hormone the only satisfactory method is to measure the amount of its excretion product pregnandiol in the urine.

In the case of the urinary androgens the capon's comb test is the method of assay of most value the seminal vesicle test being complicated by the fact that foreign substances not in themselves androgenic augment the effect of the androgens. These so called X substances do not affect comb growth. There are two related substances occurring in the urine and possessing androgenic activity normal androsterone and trans dehydrosterone. These two compounds can be found in the urine of both sexes. For these reasons the comb growth promoting activity of urinary extracts may not be an index of the production of androgens because these extracts are probably a complex mixture of degradation products.

Zimmermann has elaborated a colorimetric test and Callow and co workers a spectrographic test. Neither of these chemical methods of assay bear as yet a close relation to the biological activity of the substance under investigation.

As regards the measurements of androgens and oestrogens in the blood in the author's opinion quantitative assays at the moment seem impossible. While some progress has been made with the oestrogens the limited quantity of blood available and the small amount of oestrogen to be assayed makes this problem even more difficult than the analysis of urine.

RESULTS OF RADIUM TREATMENT OF CANCER OF THE UTERINE FUNDUS WITH SPECIAL REFERENCE TO THE MICROSCOPIC GRADE OF THE LESION

Between 1925 and 1935 of 330 patients with carcinoma of the fundus presenting themselves for treatment 115 or slightly more than a third, were treated entirely with radium or with radium and X-rays. The average age of the group was 60.6 years. In most of the cases operation was not performed because of the presence of other serious disease, such as obesity, cardiovascular disease, secondary anaemia and diabetes. In 24 per cent of the patients no concurrent disease was present but the lesion was considered inoperable.

The cases were divided into four stages. In Stage I the lesion was limited to the cavity within the level of the internal os, the uterus was moveable and not enlarged. In Stage 2 the uterus was increased in size but still moveable. In Stage 3 there was definite infiltration of the parametrium and partial fixation of the uterus. In Stage 4 the uterus was enlarged and completely fixed or remote metastases were present.

As many of the patients had been previously treated by the cautery, radium or X-rays they were divided into a primary and a modified group. Of the 93 primary cases 57 per cent were in Stages 3 and 4, of the 16 modified cases 75 per cent were in Stages 3 and 4.

Considering the primary and modified cases together the total five-year survival rate was 39 per cent and for each stage as follows: 93 per cent in Stage 1, 52 per cent in Stage 2, 34 per cent in Stage 3, 6 per cent in Stage 4. The five-year survivals were 43 per cent in the adenocarcinoma group, but only 17 per cent in the case of squamous carcinomata. The five-year survival rate also showed a relation to the grade of malignancy, the rate decreasing as the microscopical grade of the tumour, as measured by Broder's criteria, increased. The slow growing and supposedly radio-

resistant Stage 1 and 2 tumours responded better than the Stage 3 and 4 growths, in contrast to the generally accepted opinion based on carcinoma of the cervix.

The paper does not give technical details. A divided dose technique was used, brass tandems containing the radon being inserted first in the fundus and then on successive treatments, in the mid portion and the anterior portion of the canal.

THE ELECTROLYTIC THERAPY OF PREMENSTRUAL DISTRESS

The authors treated 40 women suffering from premenstrual distress, headaches, irritability, abdominal distension, nausea, etc., with ammonium chloride, given in doses of one gram three times a day for 10 to 12 days before the onset of the period. In order to limit the sodium intake somewhat the patients were asked to refrain from using table salt during the treatment. Thirty-four of the patients experienced definite relief and said they had an increased sense of well-being. The treatment gave no relief to patients complaining of migraine, dysmenorrhoea or mastodynia.

The hypothesis is that the treatment exerts its effect by reducing salt and water retention in the premenstrual phase. The work of Frank, Thorn and Emerson, Israel and others suggests this retention is due to the action of progesterone or progesterone plus steroids, and although further evidence is required it appears that the responsible steroids are elaborated by the corpus luteum.

Ammonium chloride is not specific in the electrolytic therapy of premenstrual tension. Other salts which can displace or withdraw sodium may be equally effective.

INFUSIONS OF BLOOD AND OTHER FLUIDS VIA THE BONE MARROW

The authors describe their experience with intramedullary transfusion. They have practised it in 11 infants. They give full details of their technique and results.

In children under three years of age the sternum is not a suitable bone and the injection should be made into the tibia. The most usual difficulty encountered in the method is choking of the needles by the marrow. The two failures were in cases of congenital anaemia and erythroblastosis, and the failures might be attributable to the abnor-

mal degree of ossification met with in this disease. In the nine successful cases citrated blood and salines were given when intravenous transfusions would have been impracticable. No local or constitutional reactions were disclosed by clinical and radiological examination.

OXYGEN TENT THERAPY IN THE TREATMENT OF ECLAMPSIA

The author considers treatment of eclamptic patients with an oxygen tent of great help in restoring consciousness. All his 13 patients recovered, 9 of them with a living child. Oxygen tent therapy was used to supplement a modified Stroganoff technique combined with restriction of fluids. The method takes effect by combating the anaemia of the disease.

THE SYNTHETIC OESTROGEN DIETHYLSTILBOESTROL

Diethylstilboestrol therapy gave good relief of hypogonadal symptoms in 128 out of 150 women (85 per cent). The best routine was found to give 1 mgm of the drug daily by mouth for 14 to 21 days followed by suspension of treatment for 7 to 14 days. The minimal effective dose should however be used and in some cases 0.3 to 0.5 mgm daily for 2 to 3 weeks is an adequate monthly requirement. Liver function, blood and urine studies showed no toxic effects.

The authors prefer an intermittent to a continuous administration because of the prolonged bleeding which often occurs during continuous treatment and is almost certain to occur on cessation of treatment. The time of this bleeding cannot be predicted whereas with the interrupted method the artificial menstruation occurs 5 to 12 days after stopping the drug and lasts as a rule for only 3 to 7 days. Subjective improvement and favourable vaginal smears also persist during the period of omission of the drug.

TREATMENT OF THE MENOPAUSE EVALUATION OF OESTROGEN IMPLANTATION

The authors treated a series of 180 women at the menopause both natural and artificial by implanting both loose and compressed crystals of a oestradiol, a-oestradiol benzoate and a oestradiol dipropionate. A control series of 18 patients was given a single injection of comparable amounts of oestrogen in oil.

The effects of the treatment were judged by the degree of symptomatic relief, the intensity of the proliferative changes in the endometrium and the vaginal mucosa and the duration of hypophyseal inhibition as indicated by the suppression of gonadotropic hormone excretion. Judged by these criteria the implantation of oestrogens in the form of loose crystals or pellets is more efficient than the use of injections of the hormones in oil. The longest period of symptomatic relief was obtained by the implantation of 1 oestradiol crystals.

SPONTANEOUS PNEUMO MEDIASTINUM IN THE NEW-BORN

Eight cases of pneumo mediastinum in new-born children have been described since Stransky's review of the subject in 1928. The present authors record 4 further cases. The details of the first are as follows.

The child, a male weighing 9 pounds, was born normally, required no resuscitation at birth and cried normally. Thirty hours after birth the child suddenly became cyanosed with distended neck veins and a respiratory rate of over 130 a minute. No abnormal breath or heart sounds were heard. There was no subcutaneous emphysema or precordial bulging. Immediate X-ray films established the presence of a pneumo mediastinum. Twenty-four hours later the child's condition became worse and fresh X-rays showed an increase in the amount of mediastinal air. A 21 gauge needle attached to a 20 c.c. Luer syringe was inserted into the third left interspace 1 cm. to the left of the edge of the sternum and directed medially. The plunger of the syringe suddenly moved to the 6 c.c. mark and within 5 minutes the child's condition dramatically improved. An X-ray taken 10 minutes after the aspiration showed that approximately 70 c.c. of air had been removed.

In one of the author's subsequent cases a spontaneous pneumothorax was observed to follow the pneumomediastinum.

In discussing the cases the authors stress the value of a lateral radiogram. The typical appearances are one or more pools of encapsulated air just beneath the sternum. In general treatment should be conservative, oxygen and stimulants being given as required. Increasing dyspnoea and cyanosis may call for therapeutic aspiration.

PERCY MARRAS

THE Journal of Obstetrics & Gynaecology of the British Empire

VOL 30, No 6

NEW SERIES

DECEMBER, 1933

A Review of the Problem of Purpura During Pregnancy

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THE occurrence of purpura during pregnancy has been observed and studied for many years and yet the total number of recorded cases is very few. The first was described by Barnes¹ in 1867, since when a new case has been reported about once each year raising the total number to 75. Of these we have been able to trace descriptions of 68. The majority of these reports are presented with a paucity of clinical data and an absence of pathological facts which greatly detract from their value, blood counts are quoted in a minimum of cases, with the result that one is unable to appreciate either the type or the cause of the purpura described. At the same time, the early observers did not hesitate to quote mortality-rates for the disease and to formulate laws of its occurrence. We believe that many of these laws are only rough approximations to the truth, and we have taken the opportunity of describing a case of purpura complicating pregnancy which came into our care, and at the same time subjecting previous literature on the subject to a thorough analysis, in an endeavour to

arrive at a truer conception of the features of this disease complex.

Purpura, even apart from pregnancy, is a condition which is still imperfectly understood though it can be classified into certain categories which most authorities find acceptable. Thus, as stated by Whitby and Britton,² there are three main types.

1 Purpuras showing quantitative deficiency in platelets (below 40,000 per c mm.)

2 Purpuras with slight or no deficiency in platelets

3 Purpuras due to a qualitative deficiency in platelets

The first group comprises idiopathic essential thrombocytopenic purpura and malignant purpura due to bone marrow defect. In both conditions multiple haemorrhages occur into the skin or from the mucous membranes, bleeding time is prolonged, clotting time is normal and clot retraction is poor. In the essential form the reduced number of platelets may be caused either by an absence of maturation of megakaryocytes, which though present in normal

numbers themselves are inhibited by a substance derived possibly from the spleen or the platelets may be produced normally but destroyed as they circulate through the peripheral vessels and the spleen. Although the degree of purpura is proportional to the lack of platelets, the tone of the capillary walls also plays some part, as Macfarlane³ has shown that the capillaries in such cases have a damaged endothelium, a defective contractility and malformed loops.

In the form known as malignant purpura, the reduction of platelets is due to a diminution in the number of megakaryocytes, often to an enhanced degree, which may occur alone or in association with a generalized bone marrow defect such as occurs with aplastic anaemia, medullary carcinomatous deposits, and with poisoning by benzol, novarsenobillon, etc.

The second group of purpuras comprises simple symptomatic purpura which is mainly due to a toxic degeneration of the vascular endothelium. Such drugs as belladonna, quinine and sulphapyridine may here be cited while a lack of vitamin C and vitamin P has the same effect. Anaphylactoid purpuras associated with urticaria, joint pains, oedema and visceral disturbances are included in this group. In these conditions the bleeding time, clotting time and clot retractility are normal.

Finally in the third group the platelets though normal in number are of deficient quality and disintegrate so easily as to cause purpuric symptoms. These conditions, typified by Glanzmann's haemorrhagic thrombasthenia and von Willebrand's thrombopathy, are essentially hereditary and encountered only infrequently.

When past observers have collected a series of cases of purpura of pregnancy, they have made no attempt at classification. Thus they have grouped together purpuras of all three types and have drawn conclusions from them as a whole. Rushmore⁴ in

1925 stated that the mortality-rate of purpura of pregnancy was 59 per cent for the mother (out of a total of 44 cases) and 64 per cent for the child (42 cases), he also concluded that it was more frequent in multiparae (28 out of 35 cases), and occurred chiefly during the later months of pregnancy (28 were in the last 3 months out of 38 cases). These conclusions we venture to suggest are but statistical averages of the true facts. The incidence, prognosis and mortality-rate of purpura will differ, in the same manner as statistics concerning any particular symptom will differ, according to the type of purpura concerned. In an endeavour to paint a more correct picture we have classified the 68 traced cases into the above three categories of Whitby and Britton, and from a study of each group separately we can hope to obtain information of a more helpful and accurate character. In our attempt to do this we have met with great difficulty, as the platelet counts have been recorded only 12 times, and the bleeding and clotting times still less frequently. However, in spite of this, the clinical histories are in some cases so detailed as to leave no reasonable doubt as to the cause of the purpura. Table I contains 22 cases of purpura of pregnancy in each of which the cause of the purpura has been ascertained with a fair degree of accuracy, the remaining 46 we have had to omit as being of too doubtful aetiology.

Purpura is well known to be a rare association of pregnancy, but a study of Table I reveals the extreme rarity of true essential thrombocytopenic purpura even among the recorded cases. Only 4 of the 68 cases can be accepted as examples of this condition. Cases exhibiting qualitative platelet defect are also rare as would be expected from the infrequency with which these conditions are encountered. It is interesting to note incidentally that cases have not been reported from the Baltic area, for it is there that

REVIEW OF THE PROBLEM OF PURPURA DURING PREGNANCY

TABLE I

Case	Year	Parity of mother	Duration of pregnancy	No of platelets	Fate of mother	Fate of child
GROUP I						
1 Lichling ^a	1926	1	5 months	10-300 000	Full recovery in 3 months	Full recovery in 3 months
2 Siegler ^a	1931	5	Postmature	80 000 BT-1 minute CT-1½ minutes CRF-2½ hours	Recovered	Died at 1 day ^a
3 de Saussure and Townsend ⁷	1935	0	Term	33 000 BT>30 minutes CT-5½ minutes	Full recovery	Stillborn
4 Bernstein and Newman and Hitzig ^a	1939	1	5 months	10 000 BT>10 minutes CT-13 minutes	Full recovery	Normal, but died from atelectasis
5 Posner ¹⁰ (due to quinine)	1937	2	Postmature	17 000	Full recovery	Purpura at birth Platelets, 10,000 Recovered later
(b) Bone marrow defect						
6 Barnes ¹ (associated with rheumatism)	1867	-	6 months	-	Died	Died
7 Rushmore ¹ (associated with arthritis)	1925	1	6 months	13 500 (very anemic)	Full recovery	Stillborn No purpura
8 Long and Orr ¹⁰ (associated with rheumatism)	1910	2	Term	-	Recovered	Normal
9 Vignas and Strissman ¹¹ (associated with syphilis)	1921	3	Term	-	Recovered	Normal
10 Pechen and Miller ¹⁰ (due to quinine)	1931	3	- months	130 000 BT-3 minutes CT-4 minutes	Recovered	Therapeutic abortion
11 McCoog and (anti syphilitic treatment)	1935	-	7 months	155 000	Recovered	Stillborn (due to recurrent hemorrhage)
GROUP II						
(a) Anaphylactoid						
(b) Symptomatic						

GROUP II—Continued

TABLE I—(Continued)

Case	Year	Parity of mother	Duration of pregnancy	Term	No of platelets	Fate of mother	Fate of child
12 Stone and Bumma (due to quinine)	1936	1					
13 Israel and Winsom (due to hyperthyroidism)	1911	1	6 months		Normal BT—2½ minutes CT—3 minutes	Recovered (followed by acute yellow atrophy)	—
14 Wiener (fever unknown probably smallpox)	1887	1	7 months		140 000 BT—normal CT—normal	PPH recovered	Stillborn triplets
15 Ilanet and Lucret (Streptococcal septicaemia and meningitis)	1891	1	Term		—	Died	Died
16 Leclercq (fever unknown but polymorphs 86 per cent)	1908	5	6 months		—	Died	Died
17 Ferrom	—	—	—	—	—	Died	Died
18 Zingencster	1898	1	6 months	—	—	Recovered	Normal
19 Mosher	1923	6	7 months	—	—	Recovered	Died
20 Walther	1921	1	7 months	—	—	Recovered	Died
21 Sanford Leshe and Crane	1936	1	Term	—	—	Recovered	Purpura at birth
22 Davidson	1937	1	Term	10 000	Healthy but platelets low	Purpura at birth Platelets 20 000	Purpura at birth Platelets 28 000 Normal at 2½ years

(1) Qualitative platelet defect

(d) Due to scurvy

(c) Due to fevers

most observations of these diseases have been made

The most common types of purpuric changes that occur in pregnancy are the symptomatic purpuras, appearing in association with rheumatism, drug intoxications, fevers and scurvy. The last disease must have been a common cause of purpura of pregnancy in past decades, for Mosher²¹ writing in 1923 describes what Rushmore calls "the best composite picture of the clinical course of pregnancy complicated by purpura" as follows

"Her gestation shows no untoward symptoms until some time in the 6th or 7th month she experiences a vague discomfort, loses appetite and complains of headache, she has palpitation and gastro-intestinal trouble which becomes more marked. Some time later there appear haemorrhagic spots on the skin, then petechiae, which are at first discrete, but later become confluent. These spots usually appear in successive crops. The woman finds that her gums are tumefied and painful and begin to bleed, epistaxis becomes troublesome, she usually has a persistent diarrhoea, she consults a doctor who finds that the foetus is living but the mother has purpura with symptoms of grave character."

It is evident that this is a description of scurvy in a pregnant woman, and cannot be accepted therefore as an example merely of purpura. In view of recent knowledge gained as to the prevalence of sub-clinical scurvy at the present day, it may be concluded that many of the past cases were due to this cause. Thus it is probable that one of Ferroni's¹³ cases and those of Zange-meister²⁰ and Mosher²¹ were of this nature, there is little doubt that a number of the 46 unclassified cases also belong here, as it can be fully appreciated that the extra strain of pregnancy thrown on a mother near the borderline of vitamin C insufficiency would easily precipitate her into a scorbutic state,

and produce what Rushmore quotes as a "typical" example

In a similar manner the case described by Hanot and Luzet¹⁷ cannot be considered to be primarily a case of purpura of pregnancy, it is essentially a case of streptococcal meningitis and septicaemia with purpura, in which the pregnancy is purely incidental. In the cases described by Vignes and Stiassnie¹¹ and McCoogan,¹ drugs used for anti-syphilitic treatment appear to have been the causal factor, while in those reported by Posner,⁹ Peshkin and Miller,¹² and Stone and Bunim,¹⁴ quinine has apparently exerted a noxious influence on the bone marrow, even producing in Posner's case an actual thrombocytopenia of 17,000. Many of the unknown cases probably resulted from the use of these drugs, owing to the past higher incidence of syphilis, and the extensive use made of quinine as an abortifacient and in medical inductions of labour.

We have recently had under our care a case of purpura of pregnancy which we have been able to study in some detail, and which we believe to be an example of true thrombocytopenic purpura. As this is only the fifth case which we can discover since 1867, we feel it will be of advantage to describe the clinical picture and the pathological features which it presents

CASE REPORT

Mrs J W was a primigravida aged 21, who first attended the antenatal clinic on June 6th, 1942 when she was 11 weeks pregnant. Her previous history was good, and did not contain anything of clinical note and abnormal clinical findings were not present on examination. The family history was equally uneventful except for the fact that her father had contracted malaria during the last war. The husband's family and personal medical histories were similarly devoid of clinical interest.

J W next attended the clinic on June 30th 1942 when she was 14 weeks pregnant and complained

of epistaxis which had commenced 4 days previously and had lasted for 2 days. Her general health was good and there had not been any morning vomiting. Examination revealed extensive and widespread ecchymoses and crops of petechiae present on the chest, abdomen, arms, thighs and ankles, all of these had spontaneously appeared about the same time as the epistaxis. Intensive questioning did not reveal any history of a previous similar attack and detailed enquiry as to her diet did not show a deficiency of any of the food values. There was no evidence of pregnancy toxæmia. The patient was admitted for investigation and treatment.

In hospital close clinical examination failed to reveal any abnormal physical signs apart from those already mentioned. The circulatory, respiratory and nervous systems were normal, the mouth and gums did not show any pathological changes, the spleen was not palpable, and there were no enlarged lymphatic glands to be felt. The patient had not been taking any drugs. Her blood-pressure was 124/75 mm Hg and her blood count on admission was as follows:

Red-blood cells, 5,060,000 per c mm, white blood

A provisional diagnosis of thrombocytopenic purpura complicating pregnancy was made but active treatment was not instituted as further bleeding did not occur. The following investigations were carried out with the results shown:—

Wassermann reaction negative, plasma fibrinogen 310 mgm per cent, blood ascorbic acid 0.47 mgm per cent, blood prothrombin time 3 minutes 45 seconds (Howell), red-cell fragility, within normal limits, blood calcium 12.8 mgm per cent.

Sternal puncture showed a normal picture (see below). Microscopy of the urine revealed some red blood cells and there was a trace of occult blood in the faeces. Harris and Ray's ascorbic acid saturation test showed no deviation from normal, the results being similar to those obtained in three apparently healthy controls. Unfortunately practical difficulties prevented us from carrying out estimations of pregnandiol excretion.

As there were no further haemorrhages and the original ecchymoses had regressed, the patient was discharged, advised to take supplementary vitamin therapy and kept under supervision at the antenatal clinic. Progressive platelet counts were carried out and the results are shown in Table II.

TABLE II

Date	Period of pregnancy, in weeks	Platelet count per c mm	Tourniquet test
July 2nd, 1942	14	15,000	Positive
July 3rd, 1942	14	Practically absent	Strongly positive
July 10th, 1942	15	21,000	Positive
July 23rd, 1942	17	62,000	Positive
August 6th, 1942	19	102,000	—
August 12th, 1942	20	145,000	Positive
September 8th, 1942	24	138,000	—
October 20th, 1942	30	160,000	—
November 10th, 1942	33	127,000	Positive
November 28th, 1942	35	163,000	—

cells, 8,000 per c mm, differential count normal, haemoglobin 82 per cent, colour index 0.82, platelets, 15,000 per c mm, no abnormal forms seen.

Bleeding time (BT), 27½ minutes, clotting time (CT), 4 minutes, clot retractility delayed, Tourniquet test, strongly positive.

Apart from the regular appearance of fresh petechiae and ecchymoses, the patient's health remained excellent during the later months of her pregnancy and no further external bleeding occurred.

On January 2nd, 1943, the patient was delivered of a healthy female child weighing 7 pounds 14

ounces, following a labour lasting for only 6 hours with a 1st vertex presentation. Despite a perineal laceration of the second degree the mother's postpartum loss was slight. The infant bore no evident stigmata of purpura and the placenta appeared normal. At the time of delivery the mother's platelets were 76,000 and those of the placental blood were stated to be in excess of 121,000, an accident preventing the true figure being ascertained. Afterwards mother and child progressed satisfactorily and the puerperium was normal. At the end of the first week the mother's platelets had risen to 105,000, bleeding time was 4 minutes, clotting time 4 minutes, and the tourniquet test was weakly positive. The infant's platelets were then 332,000. She was discharged from hospital on the 12th day after delivery when the perineum was healed, the lochia were scanty and colourless and the uterus was anteverted and normally involuted. Petechiae were not present and breast feeding was well established. The umbilical cord had separated on the 6th day, the umbilicus was healed and the weight of the child on discharge was 7 pounds 10 ounces.

Seven weeks after delivery the mother was seen at the postnatal clinic when although she was obstetrically normal and still had amenorrhoea a few petechiae were visible on the abdomen and thighs and she stated that she had had slight epistaxis. A blood count taken at this time revealed that her platelets were 162,000, later 3 months after delivery, when her symptomatic recovery was quite complete they were 174,000. The baby was then thriving normally and had a platelet count of 345,000.

CONCLUSIONS

There can be no doubt that this case was one of true thrombocytopenic purpura complicating pregnancy, for in addition to the diminished number of platelets the bleeding time was prolonged, the clotting time was normal and clot retraction was poor. The clinical course of the disease and the normal appearances upon sternal puncture exclude the possibility of malignant purpura, while the absence of peripheral symptoms eliminate a purpura of the anaphylactoid type.

No noxious drugs had been taken, no fever had occurred, there was no syphilis, the blood ascorbic acid test and the vitamin C saturation tests rule out the possibility of scurvy. The condition was not inherited and no question of Glanzmann's thrombasthenia or allied complaint can be raised. In addition the blood chemistry was normal, as the blood calcium, fibrinogen, prothrombin and cell fragility all show.

The salient features of the 4 recorded cases of true essential thrombocytopenic purpura, those of Liebling,⁷ Siegler,⁸ de Saussure and Townsend,⁹ and Bernstein, Newman and Hitzig⁵ are included in Table III for comparison with the present case.

From the facts portrayed in Table III and those presented in the case report it is possible to form the following conclusions.

Family history. Antecedent family history of purpura was not apparent in any case, in one instance only was it stated that the patient's mother bruised easily.

Age and Parity. The condition can occur at any age within the child-bearing period, and in association with any degree of parity.

Health prior to pregnancy. In only one case (the one in which the mother's bruising occurred) was any haemorrhagic tendency noted.

Health in previous pregnancies. In both cases noted this was normal.

Health during reported pregnancy. In one case petechiae were first observed in the early weeks and haemorrhages occurred later in the pregnancy, in our case at 14 weeks, in 2 cases at 5 months, in only 1 case did the bleeding start at term. The number of platelets varied considerably, in Liebling's case and in ours they fell in mid-pregnancy and rose again during the third trimester, in spite of the absence of very active therapeutic measures. In Bernstein, Newman and Hitzig's case they rose similarly but only in the customary manner after splenectomy. Contrary to their con-

TABLE III

CASE	LIEBLING	SIEGLER	DE SAUSSURE and TOWNSEND	BERNSTEIN NEWMAN and HITZIG
Family history	Negative for haemorrhagic tendency	Mother bruised easily	Not stated	Not stated
Age	22	29	35	23
Health prior to pregnancy	Not stated	Menorrhagia Subject to black and blue spots for 7 to 8 years	Not stated	Bilateral otitis media and sinusitis Periods normal
Parity	I	5	9	I
Health in previous pregnancies	Not stated	Postpartum haemorrhage after 4th labour otherwise normal	Normal	Not stated
Health during pregnancy	Petechiae appeared at 5 months with bleeding from gums and epistaxis Platelets 40 000 at 6 months 300 000 at 7 months	Spots noticed by patient at 5th month Not seen by doctor until at delivery Platelets 80 000 BT—1 minute CT—1½ minutes CRT—2½ hours	Bleeding from mouth and vagina on day before delivery Platelets 33 000 BT>30 minutes CT—3½ minutes	Petechiae in early weeks Vaginal haemorrhage and epistaxis at 5th month Platelets 10 000 BT>10 minutes CT—13 minutes Splenectomy at 24 weeks Platelets then rose to 220 000
Labour	Normal Amount of bleeding not stated	Postmature No tear Loss of 1½ litres of blood	Normal Moderate bleeding	Two months premature Normal 30 c c blood lost
Puerperium	Platelets 20 000 on 4th day BT—4½ minutes CT—5 minutes	Petechiae faded by 5th day	Platelets 52 000 after delivery	Normal Daily blood counts normal
Child	Platelets 40 000 Petechiae present at birth These faded no new ones appeared	Died at 4th day No postmortem or blood count recorded Presence of purpura not stated	Stillborn Presence of purpura not stated	Normal but premature Platelets 170 000 Died at 8 days from atelectasis
Follow-up	Petechiae present on mother up to 2 months postpartum Fully recovered at 3 months	Platelets 80 000 at 6 weeks 120 000 at 22 weeks	Platelets 130 000 in 4 weeks 237 000 in 26 weeks	Platelets 180 000 at 43 days Thereafter full recovery
Treatment	Ca lactate and ferrous carbonate	30 c c husband's blood Liver extract Sunlight Haematinic diet	Horse serum X ray treatment Anti venom Intravenous glucose Iron copper and arsenic	Blood transfusions Iron and vitamins A B D Moccasin snake venom Splenectomy at 24 weeks

clusion, it is evident that improvement in the blood picture can occur apart from this operation. In the case described by Siegler, although the patient noticed spots at the 5th month, when presumably the platelets

must have been few, a count was not made until delivery, when in the absence of any previous treatment they were 80,000. The thrombocytopenia thus usually appears early in the pregnancy.

Labour The amount of blood lost at the confinement varies from case to case, apparently haemorrhage may occur, but in no case is it very alarming—in our patient, despite a perineal laceration, it was slight. The haemostatic effect of efficient uterine retraction is evidently still the factor of paramount importance in these thrombocytopenic cases.

The puerperium After delivery in all cases the petechiae faded and the platelet count rose, though in 2 cases, Liebling's and ours, fresh petechiae did appear during the first 2 months, however, within periods varying from 3 to 6 months all observers record the mother's full recovery.

The child No rule can be laid down about the fate of the child. Of 5 cases 3 infants died, but apparently not from purpura. Siegler's case may be an exception as he states that the probable cause of death was purpura haemorrhagica, but he does not record that petechiae were present, no blood count was made and no postmortem examination was performed. The case we have reported shows that it is quite possible for the pregnancy to terminate in the birth of a healthy child with a normal blood count.

The reported cases in which the child develops purpura (Rushmore quotes 7 out of 47 cases) are probably either examples of symptomatic purpura in which the child is subjected to the same influence as the mother, such as quinine in Posner's case, or else they are examples of familial platelet defect.

Treatment All 5 cases had completely different treatment and all recovered. Probably, therefore, the treatment has little influence on the complaint. Bernstein *et al* form the conclusion that splenectomy is necessary for the birth of a healthy child, our case shows that this is not so. They also suggest that the absence of postpartum haemorrhage is due to the splenectomy, a

fact which our case again disproves. It thus appears that the indications for this operation are the same as obtain in purpura apart from pregnancy.

Sternal puncture Sternal punctures are recorded in only 2 cases with results as follows.

BERNSTEIN, NEWMAN and HITZIG

Cell count	250,000
Megakaryocytes	13.2 per cent
Myeloblasts	1.4 "
Myelocytes	29.4 "
Polymorphonuclear leucocytes	18.8 "
Lymphocytes	1.0 "
Other cells	6.2 "

PRESENT CASE

Cell count	Normal cellularity, not very active
Megakaryocytes	3/500 nucleated cells
Myeloblasts	1.0 per cent
Myelocytes	7.4 "
Polymorphonuclear leucocytes	50.4 "
Lymphocytes	20.4 "
Eosinophils	1.6 "
Metamyelocytes	5.2 "
Plasma cells	0.2 "
Monocytes	0.6 "
Normoblasts	11.8 "
Pro-erythroblasts	1.2 "
Haemocytoblasts	0.2 "

Apart from the excess of megakaryocytes in the former case both counts are stated to be within normal limits.

DISCUSSION

The relation between purpura and pregnancy still remains obscure. We do not know whether the patients exist all their lives with a low platelet count which the strain of pregnancy reduces to below the purpuric level of about 40,000, or whether they are completely normal individuals who are subjected to a pathological process during their pregnancy which produces purpura. As the strain of previous pregnancies in the multiparae does not appear to have precipitated purpura, it seems likely

that the latter contention is the correct one. In either case we have no idea what this "strain" or pathological process that produces the thrombocytopenia actually is. It is true that earlier workers have reported examples of recurrent purpura of pregnancy but on close examination these have proved to be cases of symptomatic purpura, such as the case of Vignes and Stiasnie¹¹ in which purpura occurred during 3 successive pregnancies in a syphilitic woman. In hereditary purpura also the purpura is recurrent, thus Sanford *et al*²¹ and Davidson,²¹ in presenting cases of qualitative platelet defect, conclude that the platelets possess an increased disintegrative ability and so produce purpura when the patient is subjected to increased strains of life such as pregnancy. In these cases, however, the condition is familial in a manner that true purpura is not.

We must also consider the possibility that the purpura and the pregnancy are unrelated causally, and that the patient who suffers from purpura haemorrhagica and is subject to periodic relapses chances to have one which coincides with pregnancy. The extreme rarity of the association somewhat suggests this view, but as each of the 5 cases did not give any history of a previous relapse, and each made a complete symptomatic recovery within 3 to 6 months after delivery, it is impossible not to conclude that the two conditions are correlated in some manner. Observation of the subsequent progress of these cases might however reveal that the recovery is transient and that further relapses are liable to occur, in this event the association with pregnancy must be considered fortuitous. It is true no such case has yet been reported to the best of our belief, but until these accepted cases have been watched for many years and then continued recovery confirmed, we cannot deny that such an occurrence is possible.

Some authors speak of purpura being due to a toxæmia of pregnancy, Kosmak² and Seitz²⁶ stating that it occurs in association with hyperemesis gravidarum and eclampsia. This association must be most rare in view of the great frequency with which these two toxæmias are encountered, and moreover in those cases which have been reported the purpura is of the non-thrombocytopenic variety. Purpura occurring in toxæmia of pregnancy is of the symptomatic type, and whether the two are causally related or purely coincidental is problematical, and does not concern our consideration of true purpura, in cases of which, as we have shown, evidence of these toxæmias is completely lacking. Liebling suggests that his case may be due to toxæmia but offers no support for his statement. If we do accept a toxæmia theory we must hypothecate an independent form of metabolic toxæmia, such as what Siegler terms a "latent toxæmia," affecting only the platelets. We do not ourselves accord much support for such an assumption, because not only is its occurrence extremely rare, but the purpura begins very early in pregnancy and has a distinct tendency to improve in the absence of treatment as the pregnancy progresses, which is unusual for a toxæmia.

An interesting speculation has been opened up by the work of Pohle² who has shown conclusively that the platelet count varies with menstruation, being lowest before the onset of the bleeding. After careful analysis he suggests that the cause of this may be hormonal in nature. If this be so it is evident that the increased hormonal fluctuations of pregnancy may in certain circumstances reduce the platelet count still further and give rise to the onset of purpura. Pfeiffer and Hoff²⁸ have demonstrated that a thrombocytopenia may result from the action of progesterone on the spleen, and should this hormone be produced in quantities greater than the normal for preg-

nancy, we suggest it may cause a reduction to purpuric levels. It is for this reason we regret our inability to carry out pregnandiol excretion estimations in our case. The early occurrence of thrombocytopenia and its tendency to disappear later in pregnancy, suggest that it is those hormones which reach a high concentration in the early months, such as the APL principle and the pituitary gonadotrophins, that may be responsible. In view of the normal megakaryocyte count obtained on sternal puncture we must assume that the platelet defect whatever the cause must result from either a faulty maturation of megakaryocytes which are themselves present in normal numbers, or else from their destruction as they circulate through the peripheral blood stream.

In this respect we must mention the work of Sakai²⁹ who considers that reduction in the platelet count before menstruation results from increased activity of the reticulo-endothelial system. Hyperactivity of this system during pregnancy might thus contribute to the occurrence of purpura.

Although these cases are too few in number to form a basis for definite conclusions, they do cause our views to diverge from those formulated by Rushmore in his study of purpura of pregnancy due to all causes, which have been generally accepted. These 5 cases of true purpura do not support his contention that purpura is more frequent in multiparae as 3 of them occurred in primigravidae. Again they do not conform with his opinion that purpura usually commences during the last 3 months of pregnancy, as we have demonstrated. He quotes a maternal mortality-rate of 59 per cent, de Saussure and Townsend quote one of 55.7 per cent, while in these 5 cases all the mothers recovered completely, so that true purpura of pregnancy does not appear to be a fatal disease. Certainly we do not agree with Hirst³⁰ who states that the disease is

generally fatal and always interrupts pregnancy, the foetus dying *in utero*.

We suggest, therefore, that the conclusions reached in the past do not apply to true essential thrombocytopenic purpura of pregnancy which differs diametrically from them in practically all respects, the correct picture of this complaint has in the past been disguised by the superadded features of other diseases which have been present merely as incidental causes of symptomatic purpura.

SUMMARY

1. An analysis of 68 recorded cases of purpura of pregnancy is made and in 22 cases the cause of the purpura is ascertained.

2. Only 4 cases of true essential thrombocytopenic purpura complicating pregnancy can be discovered.

3. A fifth-case of true purpura is presented.

4. The features of these 5 cases are reviewed, and conclusions are reached regarding the incidence, clinical course, treatment and mortality of the condition.

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ACKNOWLEDGMENTS

Our thanks are due to Dr W More, Medical Superintendent, Stepping Hill Hospital, for permission to publish this case, and to Professor Wilkinson, Director of Clinical Laboratory, Royal Infirmary, Manchester, for the performance of the sternal marrow count

Blood Examinations in Pregnancy

BY

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IN this paper the results of blood studies on a group of 105 women attending one of the Fulham Antenatal Clinics and the Fulham Nutrition Clinic between the end of 1936 and the middle of 1939 are reported. They were unselected. All belonged to the working and lower middle classes. Eleven cases could not be included in the general summary—6 suffered from concomitant diseases, 3 came from other clinics, 2 left the district before labour—leaving 94 cases. Of these 55 were primiparae and 39 multiparae. They were between 19 and 37 years of age. A detailed report will be published by the Metropolitan Borough of Fulham.

METHODS

Haemoglobin examinations were made with a Haldane haemoglobinometer standardized at an oxygen capacity of 18.5 per cent. Red and white cells were counted in a Thoma-Zeiss camera. The films were fixed and stained with Jenner-Giemsa solution. Red cells were dyed when wet by the azure-cresyl method.¹ Only the size of fresh wet unfixed red cells not more than slightly stained yellow was estimated because neither a Price-Jones apparatus nor a Wintrobe's haematocrit was available, and also because, in accordance with Boycott's observations,² different results were found in different parts of the stained films.

The aim of the investigation was to establish the normal physiological standards for the whole blood picture—haemoglobin, red cells, colour index and white cells, and size of the red cells, to establish their mean values for all periods of pregnancy, puer-

perium, and of the nursing and post-nursing period, and to investigate the frequency and type of the anaemias in pregnancy with regard to their aetiological agent and their response to treatment.

PHYSIOLOGICAL DATA

Any attempt to establish normal physiological standards can only be based on non-treated cases. The series of 94 cases therefore was divided into three groups as follows.

GROUP I

Cases non-treated with iron, protein, or liver during pregnancy or puerperium. Cases showing haemoglobin under 70 per cent more than once during pregnancy were not included in this group as it is generally agreed that they cannot be regarded as normal.^{3, 5, 12} 43

GROUP II

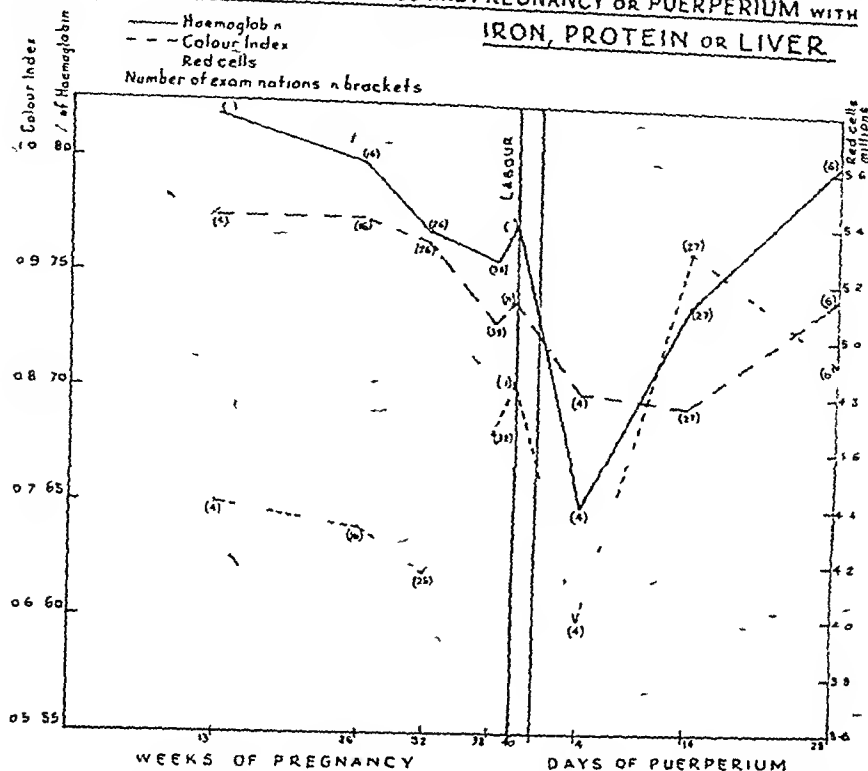
Cases treated in the antenatal clinic before first attendance at the nutrition clinic, and throughout pregnancy with routine administration of iron. 4 Blaud's pills gr xxx were given daily because they did not feel well. 7

GROUP III

Cases treated with iron, protein or liver in different periods of, or throughout pregnancy. The mean values of cases in Group III are not given because their blood picture showed different specific variations either at their first attendance or later in pregnancy and received specific treatment accordingly. 44

GROUP I 43 CASES NON TREATED DURING PREGNANCY OR PUERPERIUM WITH
IRON, PROTEIN OR LIVER

GRAPH I



WHOLE SERIES

Mean figures for the whole series of 94 cases, both treated and not treated are given for comparison with the findings of authors who do not give separate accounts of treated and non treated women during pregnancy

Mean values are given in Tables I, II, and III, and in Graphs I, II and III

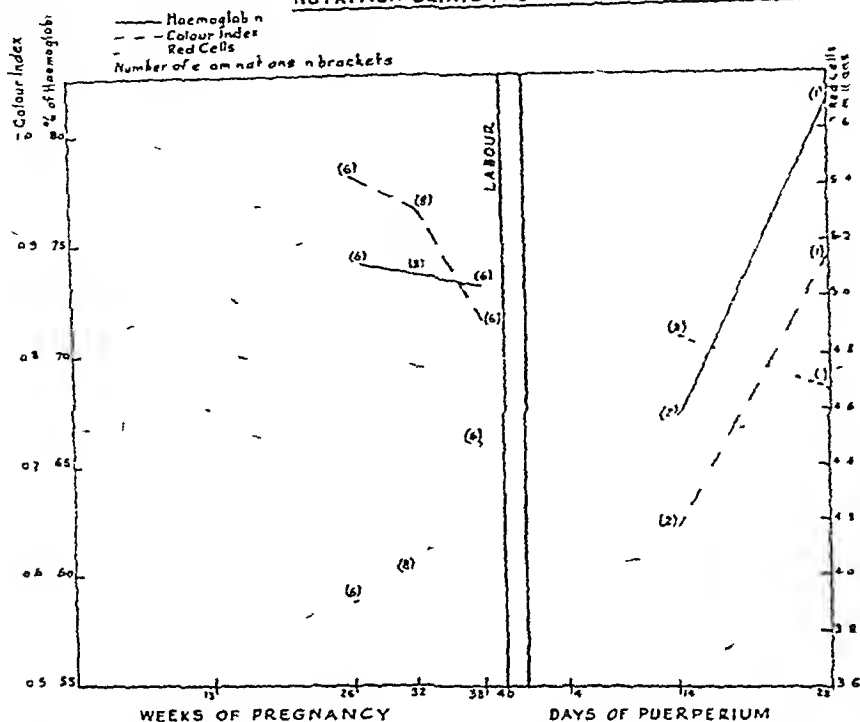
VALUES IN PREGNANCY

The results in pregnancy in general show, in agreement with Fullerton,⁴ that the haemoglobin drops with progress to term, and only rises in the 2 weeks before labour. The red cell count drops similarly in the first 6 months of pregnancy, but rises markedly and continuously in the last 3 month period taken as whole until labour. The course of the haemoglobin and the red cell count are therefore not parallel in the

last 3 month period of pregnancy. The colour index is lower in the last 3 months of pregnancy than in the first 6 months, and only recovers with the rise of the haemoglobin in the last 2 weeks before labour. Owing to the sudden sharp rise of the red cell count in the last 3 month period and the slow fall of the haemoglobin, the colour index drops substantially. The white cells are increased with progress to term up to 20,000-25,000 in conformity with the results found by other authors,⁵ and are therefore not given separately.

In order to show more clearly the differences in the non-parallel course of the haemoglobin and the red cells in the whole last 3 month period before labour, separate figures are given for the following periods (1) 27th to 32nd weeks, (2) 33rd to 38th

GROUP II 7 CASES TREATED WITH ROUTINE ADMINISTRATION OF IRON BEFORE ATTENDANCE AT NUTRITION CLINIC AND THROUGHOUT PREGNANCY



weeks, (3) 39th to 40th weeks. Some significant variations of the red cell count in the last 3 months of pregnancy will be dis-

cussed later, but the actual rise of the red cells starts in most cases in the 33rd week and goes on until labour.

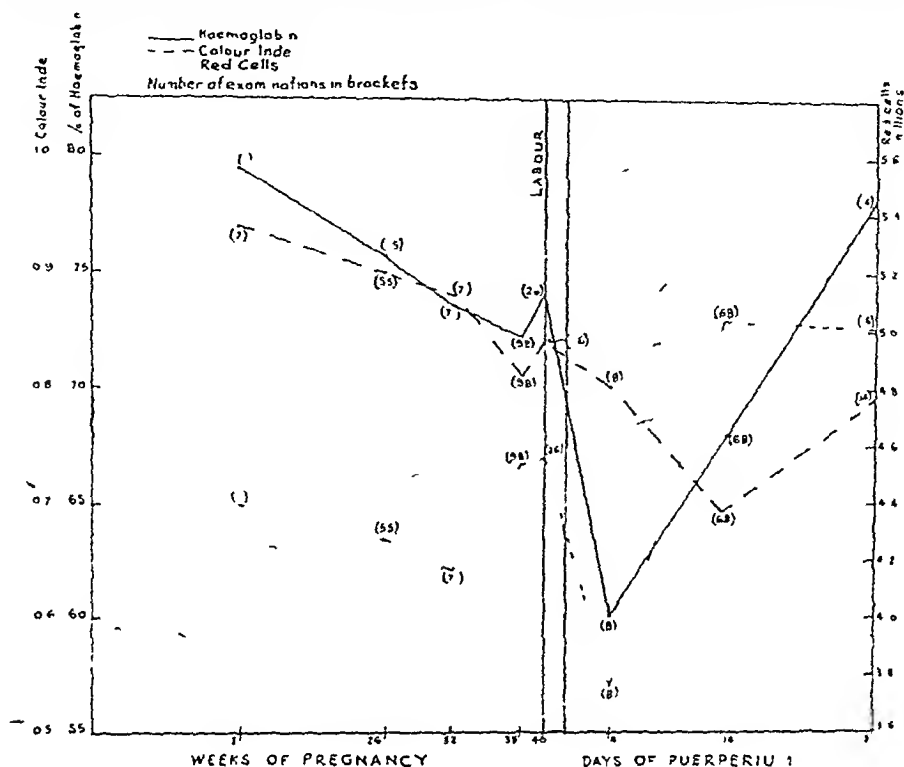
VALUES IN DIFFERENT PERIODS OF LAST 3 MONTHS

MEAN VALUES

	For whole period of pregnancy	For last 3 months	Week 27-32	Week 33-38	Week 39-40
GROUP I					
Red cell count	4.43 (95)*	4.41 (75)	4.18 (26)	4.45 (38)	4.84 (11)
Haemoglobin	78.5 per cent	76.5 per cent	77.1 per cent	75.9 per cent	77.4 per cent
Colour index	0.91	0.88	0.93	0.86	0.88
GROUP II					
Red cell count	4.14 (20)	4.24 (14)	4.03 (8)	4.49 (6)	—
Haemoglobin	73.6 per cent	73.0 per cent	73.8 per cent	73.0 per cent	—
Colour index	0.91	0.85	0.92	0.83	—
WHOLE SERIES					
Red cell count	4.39 (257)	4.36 (195)	4.17 (71)	4.54 (98)	4.55 (26)
Haemoglobin	75.2 per cent	73.2 per cent	73.5 per cent	72.3 per cent	74.0 per cent
Colour index	0.87	0.83	0.88	0.81	0.84

* Figures in parenthesis in all tables refer to number of examinations

WHOLE SERIES 94 CASES TREATED OR NOT TREATED IN PREGNANCY WITH IRON, PROTEIN OR LIVER



VALUES IN PARTURITION

During parturition the values of the haemoglobin and the red cell count in Group I (4 cases), and in the Whole Series (8 cases), drop substantially in the first 4 days after labour. No cases from Group II happened to be seen during the first 4 days after labour (see Tables I, II and III and Graphs I, II and III). It is well known^{1,2,3} that the Hb and R C C fall directly after labour. In this period only a few cases could be examined, which included patients with post-labour haemorrhage. After the first period of 1 to 4 days after labour the red cell count rises again between the 5th and 14th days inclusive after labour even above the level for the last 3 months of pregnancy, the haemoglobin level also rises but more

slowly. This divergent movement leads again to a lowering of the colour index which falls below the antepartum value, and rises again with the return to normal, i.e. the rise of the haemoglobin and the decrease of the red cells between the 15th and 28th days after labour. In these two periods of the puerperium (5th to 14th days and 15th to 28th days) the rate at which the haemoglobin and the red cell count return to normal and the colour index to unity can be considered as indices of the rate of recovery. Both haemoglobin and red cell count are tending back to normal mean values in the nursing and post-nursing periods, but in some cases the mean values in the lactation period proved to be equal to or even lower than those found in pregnancy, showing

GROUP I—TABLE I

ALL CASES NON-TREATED DURING PREGNANCY OR PUERPERIUM WITH IRON OR PROTEIN OR LIVER						Puerperium Days postpartum		
Pregnancy								
Week	12-13	14-26	27-32	33-38	39-40	1-4	5-14	15-28
Red cell count	4 41	4 32	4 18	4 45	1 84	4 01	5 30	4 93
Haemoglobin (per cent)	82 2	80 0	77 1	75 9	77 4	65 0	74 0	80 5
Colour index	0 95	0 95	0 93	0 86	0 88	0 80	0 69	0 89
No of examinations	(4)	(16)	(26)	(38)	(11)	(4)	(27)	(6)

MEAN VALUE OF ALL 43 CASES AND ALL PERIODS OF PREGNANCY

Red cell count	4 43 (95)
Haemoglobin	78 5 per cent (95)
Colour index	0 91 (95)
Total cases in pregnancy	43
Total of examinations	95

MEAN VALUE OF DIFFERENT PERIODS OF PREGNANCY

	Red cell count	Haemoglobin	Colour index
Mean value of first 6 months	4 34 (20)	80 5 per cent	0 94
Mean value of last 3 months	4 41 (75)	76 5	0 88
Mean value 39th-40th weeks	4 84 (11)	77 4	0 88
PUERPERIUM Days postpartum			
1-4	4 01 (4)	65 0	0 80
5-14	5 20 (27)	74 0	0 69
15-28	4 93 (6)	80 5	0 89
Total of cases in puerperium	30	Total of examinations	37

that recovery after delivery is not necessarily complete. This is in agreement with Mackay⁶

treated cases. The differences found in the cells in anaemic cases will be discussed later.

SIZE OF RED CELLS

The red cells in Group I were found to be constantly of average and equal size in the first 6 months of pregnancy, in the last 3 month period, with the increase in the number of the red cell count, new large cells and even megalocytes appeared, some of which were poorly haemoglobinized and showed central pallor. Anisocytosis was frequent, but poikilocytosis rare if at all. During the puerperium the cells became smaller again and more equal. The gradual return to the normal size of cells was completed in 8 to 9 months after labour, provided that pathological disturbances did not occur in the nursing or post-nursing periods. Reticulocytes were never increased in the non-

DIFFERENCES IN THE MEAN VALUES OF DIFFERENT GROUPS DURING PREGNANCY AND PUERPERIUM

The general trends of haemoglobin, red cell count, and colour index are the same in all groups. The mean fall in the haemoglobin level of Group I (non-treated) is 6.3 per cent between the 3rd and 8th months, with a recovery before term of 1.5 per cent. The corresponding changes for the Whole Series are a fall of 7.5 per cent and a rise of 1.7 per cent. The cases treated with routine administration of iron in Group II showed a drop of 1 per cent. They were only seen between the 4th and the 8th months of pregnancy, not between the 39th and 40th weeks before labour, and therefore for these weeks figures cannot be given. The routine

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GROUP II—TABLE II

CASES TREATED WITH ROUTINE ADMINISTRATION OF IRON BEFORE FIRST ATTENDANCE AND THROUGHOUT PREGNANCY

Pregnancy						Puerperium	Days postpartum	
Week	12-13	14-26	27-32	33-38	39-40	1-4	5-14	15-28
Red cell count	0	3 90	4 03	4 49	0	0	4 86	4 67
Haemoglobin (per cent)	0	74 0	73 8	73 0	0	0	67 0	81 0
Colour index	0	0 96	0 92	0 83	0	0	0 64	0 88
No of examinations		(6)	(8)	(6)	(0)	(0)	(2)	(1)

MEAN VALUE OF ALL 7 CASES AND ALL PERIODS OF PREGNANCY

Red cell count	4 14 (20)
Haemoglobin	73 6 per cent (20)
Colour index	0 91 (29)
Total of cases 7	Total of examinations, 20

MEAN VALUE OF DIFFERENT PERIODS OF PREGNANCY

		Red cell count	Haemoglobin	Colour index
Mean value of 2nd 3 months	(6)	3 90	74 per cent	0 96
Only 27th-38th weeks of last 3 months	(14)	4 26	73	0 86
39th-40th weeks	(0)	—	—	—
PUERPERIUM Days postpartum				
1-4	(0)	—	—	—
5-14	(2)	4 86	67 per cent	0 64
15-28	(1)	4 67	81	0 86
Total of cases in puerperium, 3		Total of examinations, 3		

administration of 4 Bland's pills daily to these patients prevented a further drop of the haemoglobin with progressive term but the red cell count remained in the first 6 months below the values of Group I. In the values of the red cell count in Group II an increase took place in the last 3 months. The values of the colour index were similarly lower than those in Group I (non-treated cases) in these periods. The values of the Hb, red cell count and the colour index for the Whole Series are also lower than those for Group I in all periods with the only exception of the red cell count in weeks 33-38, due to the fact that the Whole Series included all hypochromic anaemia cases in which the red cell count is less reduced than in other anaemic cases. The red cell values of the Whole Series show a rise from the 33rd to the 38th weeks, but it is significant

that the red cell count remains stationary from the 39th to the 40th weeks owing to the inclusion of anaemic patients whose red cell count deteriorated in the last weeks before labour.

CRITERIA

The mean colour index of non-treated cases in Group I attending for the first time was taken as the criterion for the normal physiological standard. In agreement with Price-Jones' findings for parous healthy women, a colour index of 0 91-1 08 was taken as the standard for women not anaemic during the first 6 months of pregnancy. For the last 3 months the standard was the observed mean value in Group I (non-treated cases) for this period, i.e. 0 88 (75 examinations). Subdividing this period, the following were taken as mean colour indices: 27th to 32nd weeks, 0 93 (26 ex-

WHOLE SERIES—TABLE III

ALL CASES, NON-TREATED AND TREATED WITH
IRON OR PROTEIN OR LIVER IN PREGNANCY

Pregnancy						Puerperium	Days postpartum	
Week	12-13	14-26	27-32	33-38	39-40	1-4	5-14	15-28
Red cell count	4 40	4 29	4 17	4 54	4 55	3 76	5 03	5 00
Haemoglobin (per cent)	79 8	75 8	73 5	72 3	74 0	60 0	68 0	78 0
Colour index	0 94	0 90	0 88	0 81	0 84	0 80	0 69	0 79
No of examinations	(7)	(55)	(71)	(98)	(26)	(8)	(68)	(14)

MEAN VALUE OF ALL CASES AND ALL PERIODS OF PREGNANCY

Red cell count	4 39 (257)
Haemoglobin	75 2 per cent (257)
Colour index	0 87 (257)
Total of cases in pregnancy, 94	Total of examinations, 257

MEAN VALUE OF DIFFERENT PERIODS OF PREGNANCY AND PUERPERIUM

		Red cell count	Haemoglobin	Colour index
Mean value of 1st 6 months	(62)	4 26	76 2 per cent	0 91
Mean value of last 3 months	(195)	4 36	73 2	0 83
Mean value, 39th-40th weeks	(26)	4 55	74 7	0 84
PUERPERIUM Days postpartum				
1-4	(8)	3 76	60 0	0 80
5-14	(68)	5 03	68 0	0 69
15-28	(14)	5 00	78 0	0 78

Total of cases in puerperium, 65

Total of examinations 82

aminations), 33rd to 38th weeks, 0 86 (36 examinations), 39th to 40th weeks, 0 88 (11 examinations). Cases with figures below these values were considered anaemic. The colour index in any one period of the last 3 months of pregnancy may occasionally be lower owing to the discrepancy between the course of the haemoglobin and the red cell count, but it was not taken as normal if it was maintained for more than 1 week and without a large and sudden increase in the red cell count. All mean values of the colour index of the Whole Series are lower than Group I (non-treated cases). The colour index in some forms of anaemia tends to unity, therefore the whole blood picture must be taken into consideration in relation to any given period of pregnancy.

PATHOLOGICAL DATA

INCIDENCE OF ANAEMIA

The 94 cases were divided into three categories according to the established standards

	No	Percentage of total cases
A Non anaemic cases non-treated with iron protein or liver	43	45 8
B Cases treated before first attendance and throughout pregnancy with routine administration of iron	7	7 4
C Anaemic cases	44	46 8
		100 0

The high incidence of anaemia (46.8 per cent in a series of 94 cases) is comparable with that found by Davidson^{8,9} in patients of similar ages and social classes (45 per cent in 3,500 cases)

DEGREE OF ANAEMIA

Out of 44 patients suffering from anaemia, 16 had a Hb level under 70 per cent more than once in pregnancy, 8 of these were patients suffering from hypochromic anaemia

Besides the high incidence of anaemia, further progressive deterioration of the blood picture was observed in the last months of pregnancy, which agrees with Smallwood's¹⁰ conclusion that occasionally severe and dangerous degrees of anaemia develop "during and as a result of pregnancy in the later months of pregnancy"

CLASSIFICATION OF ANAEMIA

The 44 cases of anaemia were classified according to their *blood picture* and their response to treatment^{11,12}. The following types of anaemia were found which may have been unconditioned, or conditioned owing to insufficient intake¹³ or defective assimilation of the diet or increased demands

	No. of cases
1 Megalocytic protein deficiency anaemia	6
2 Hypochromic iron deficiency anaemia	23
3 Pernicious anaemia of pregnancy	
(a) Hypochromic type—3 cases	
(b) Megalocytic hyperchromic type—4 cases	7
4 Vitamin C deficiency anaemia	8
	—
	44
	—

Those values were taken as representative for type and therapy which were found when the patient was first seen and before any treatment had been given (30 cases) or when anaemia developed after a normal beginning in the course of pregnancy (14 cases). In the first 6 months of pregnancy

the blood picture follows that of anaemic paucous women. Classification in the last 3 months of pregnancy was difficult because erythropoiesis was found even in hypochromic anaemic cases. As at least 3 features of the blood picture give evidence of the special type of anaemia a differential diagnosis is possible. In the last 3 month period of pregnancy erythropoiesis was found to be the dominating factor in the normal physiological non-anaemic cases of pregnancy. Although in anaemic pregnant women during this period the production of large fresh red cells is found and never quite disappears, even in hypochromic anaemia in contrast to those in anaemic non-pregnant women, erythropoiesis is disturbed in a different degree determined by the type, and in an equal ratio to the gravity of the anaemia.

VARIATIONS IN THE RED CELL COUNT IN THE LAST THREE MONTHS OF PREGNANCY

Special variations in the red cell count during the last 3 months of pregnancy were observed only in the 7 cases of pernicious anaemia of pregnancy and in 5 out of the 8 cases of vitamin C deficiency anaemia. In the above-mentioned cases after a short initial increase in the number and size of the red cells at the beginning of the last 3 months of pregnancy a distinct decrease took place during the last weeks of pregnancy, and continued until labour. This decrease of the red cell count was found in no other cases than these 12, and in no other type of anaemia in the whole series of 94. The deterioration in the red cells in number and the reduction in their size was followed by post-partum haemorrhage. This connexion was found in 10 cases out of the 12 with a defective production of the red cells in the last weeks of pregnancy. In 2 cases this connexion could not be proved as blood tests could not be made at the appropriate corresponding time.

POSTPARTUM HAEMORRHAGE

A loss of 10 ounces of free measured blood not soaked off in the towels or contained in the liquid was regarded as proof of haemorrhage. Out of 94 patients, 12 suffered from post-partum haemorrhage. Of these, 4, including 2 of Group I and 2 suffering from pernicious anaemia of pregnancy, had to be excluded either because they were not seen in the last 3 months before labour or until too long after it. Of the remaining 8 patients of measured post-labour haemorrhage, 5 had pernicious anaemia of pregnancy, and 3 vitamin C deficiency anaemia. Two further patients out of the 8 suffering from vitamin C deficiency anaemia, whose red cell count showed deterioration before labour, were assumed also to have suffered from post-labour haemorrhage, but the loss of free blood could not be measured. The red cell count of these 2 cases in puerperium was below the mean values for Group I in the same period. The loss in their haemoglobin level 9 and 13 days respectively after labour was still 11 and 17 points, which may be regarded as sufficient proof that post-labour haemorrhage had taken place. In a second series of 20 pregnant women investigated later, 2 cases of vitamin C deficiency anaemia showed a similar progressive deterioration in the red cell count before labour, and a post-labour haemorrhage of 30 ounces and 16 ounces respectively. The connexion between defective production of red cells in number and size in the last weeks before labour and post-labour haemorrhage is, therefore, not a mere coincidence, but an observation of serious prognostic importance.

THE CHARACTERISTICS OF VITAMIN C ANAEMIA

The 8 patients with vitamin C deficiency anaemia in the present series, and the 2 patients in the later series, suffered from latent scurvy, without obvious clinical

symptoms other than breathlessness, lassitude, and malaise. The values of the blood picture were used as the standard for comparison with other anaemias. The blood picture was in agreement with that recognized by Mettler and Minot¹⁴ for scurvy in adults. The red cells were more reduced than the Hb, the colour index tended to unity but was never above 1.0 as in megalocytic protein deficiency anaemia. The red cell count remained far below the mean value for Group I in the different corresponding periods. Microcytes and large red cells were observed at the beginning and during the course of the illness, megalocytes occurred rarely, if at all, in contrast to their frequent appearance in pernicious anaemia of pregnancy and in Addison's pernicious anaemia, some nucleated cells were also found. There was only slight central pallor in the large red cells, but no ringlike large cells. Microcytes were found, but not the dense-looking small microcytes found in pernicious anaemia of pregnant or of non-pregnant women. Anisocytosis was only moderate, but was seen more frequently than poikilocytosis. The failure of the blood to regenerate during the puerperium shows that the disturbing factor was still present after parturition and prevented a normal replenishment of the blood-forming elements. The reduction of the haemopoietic system chiefly affects the erythropoietic element. The values of the red cell count in the last 3 months of pregnancy and in puerperium even in patients in whom post-labour haemorrhage did not occur, were far below the normal values found in Group I, and also lower than in any other type of anaemia. The response to high dosages of iron (4 to 6 Pil Ferr Sulph) given daily at the onset of the anaemia was delayed and inadequate, and the increase of reticulocytes was also delayed. Treatment with liver was ineffective.

Harris^{15 16} and Zilva¹⁷ refer to the absence of clinical signs of scurvy in patients proved by saturation tests to be suffering from vitamin C deficiency. Clinical signs of scurvy were not found even in patients kept experimentally for months on a diet¹⁸ far below the League of Nations standard for vitamin C requirement of 30 mg ascorbic acid daily.²² Anaemia in scurvy is recognized by Mettier, Minot, and Townshend,¹⁴ by Dunlop and Scarborough,¹⁹ and by Israels.²⁰ Some authors, however, challenge this view,¹⁸ and attribute the anaemia to general under-nutrition.²¹ It is considered that anaemia is not always associated with scurvy and that if it occurs in scurvy it is not due to loss of blood.²³ In the 8 cases of vitamin C deficiency anaemia neither large doses of iron nor of liver produced any regeneration of the blood during pregnancy or puerperium. The 2 patients of vitamin C deficiency anaemia in the second series received injections of Campton 2 x 4 ccm weekly from the beginning of the deterioration in the red cell count during the last weeks before labour. These liver injections neither prevented a further decrease in the number and size of the red cells, nor a heavy post-labour haemorrhage of 30 ounces and 16 ounces respectively. Injections of 250 mg ascorbic acid 2-3 times daily had a sudden and dramatic effect in restoring normal haemopoiesis and producing a marked and rapid regeneration of the blood. In one of the two cases a relapse occurred after reduction of and full recovery after return to the former 3 dosages. The return to normal values began immediately after the injection. The increase in the reticulocytes also started after the injection and reached their peak after 20 hours in the one case seen at this period. All the blood-forming elements were restored after 12 days to the normal values for this period of the puerperium.

The improvement in the red cell count

after the administration of ascorbic acid in the 2 cases of the second series cannot be attributed to improvement in nutrition as all patients in both series received the same general diet in the Fulham Maternity Home without the addition of food rich in vitamin C. Furthermore, Szent Gyorgi²¹ *et al* have shown that pure vitamin C has a negative therapeutic action on haemorrhagic diseases of a non-scorbutic aetiology. It seems therefore permissible in the 2 cases of the second series to suggest the presence of a vitamin C deficiency anaemia dependent on continued lack of vitamin C in pregnancy and restored by a supply of the vitamin. All 8 patients of vitamin C deficiency anaemia in the first series did not receive any treatment with ascorbic acid before or after labour. The absence of improvement in the red cell count in these cases during the puerperium, whether there was post-labour haemorrhage or not, confirms once more the active presence of the aetiological factor or factors preventing normal haemopoiesis. The conformity of the blood picture in pregnancy between that given for scurvy in adults, the 2 cases in the second series and the 8 cases of vitamin C deficiency anaemia in the first series, suggests by analogy that the patients in the latter should probably be classified as suffering from vitamin C deficiency anaemia.

OBSTETRIC HISTORY

The different types of anaemia in the first series of 94 cases show widely different effects on the obstetric history of the mothers and on the children of the present pregnancy, hypochromic anaemia showing comparatively the most serious consequences. Seventeen out of 23 cases of children's diseases, dystrophy, low expectation of life, or rearing difficulties belonged to mothers with hypochromic anaemia. The 94 patients had 57 previous pregnancies, 36.8 per cent of which were a failure. There

were 7 miscarriages, 6 stillbirths, and 8 deaths of children. Four premature births are not included.

From the present pregnancies there were 6 stillbirths, 1 death (premature, died 4 months), 3 weak and prematurely born in Fulham Maternity Home and therefore included = 10.6 per cent.

DISCUSSION

A history of pre-existing anaemia was clearly defined only in 9 out of 94 patients of whom 5 showed anaemia in the present pregnancy. These 5 cases are not sufficient to justify the suggestion that anaemia in pregnancy is pre-determined. Against the assumption of Boycott² and Bethell¹² that anaemia is parallel to dilution of the blood stands the fact of the divergent non-parallel course of the haemoglobin and the red cell count in the last 3 months of pregnancy. Since the amount of the haemoglobin in the circulating blood is found to be the same throughout pregnancy, whereas the red cell count is increased, the estimation of the haemoglobin alone is not sufficient as a criterion of the frequency of anaemia. Against the contention that there is a genuine physiological anaemia in pregnancy based on the falling Hb level, stands the fact that 43 patients not treated were found not to be anaemic, having a normal colour index throughout pregnancy. The higher activity of the bone marrow with the production of new large red cells in the last 3 months of pregnancy is the determining factor of the blood picture. Pregnancy in all its complexity has the tendency to rejuvenate tissues, of which the growth of the uterus and of the foetus proper are instances. Erythropoiesis found in all non-anaemic cases of Group I is therefore a physiological factor. It is besides a consistent factor as it was also found in anaemic cases, but on a smaller, varying, and differentiating scale.

From the blood picture observed it is inferred that in 44 cases anaemia was due to deficiency of iron, protein, or vitamin C which may have been unconditioned, or conditioned owing to insufficient intake or defective assimilation. Davidson (Aberdeen) and colleagues proved in their enquiry on over 3,500 individuals that a diet containing only 6 mg iron (instead of 15-20 mg) daily produced anaemia in women of child-bearing age, but not in men.¹¹ The requirement of vitamin C in pregnancy, especially in the latter half, is 60-100 mg ascorbic acid—more than double that of non-pregnant women^{25,26}. When the requirement is not met during gestation²² the maternal organism becomes depleted for the benefit of the foetus at a time when erythropoiesis should be at its height. Thus pregnancy exerts its influence on, and intensifies such nutritional deficiency.

CONCLUSIONS

(1) Forty-three cases out of a series of 94 pregnant women were found to be non-anaemic, having a normal colour index throughout pregnancy. The 44 anaemic cases were not of a predetermined character.

(2) The movement of the haemoglobin and the red cell count, both falling, is parallel in the first 6 months of pregnancy, but definitely non-parallel in the last 3 month period with a rising red cell count and a haemoglobin falling still further until the last 2 weeks before labour. The influence of hydraemia is therefore not the determining factor of erythropoiesis in pregnancy. The higher activity of the marrow bones is the dominating physiological and consistent factor of the blood in pregnancy.

(3) A decrease of the red cell count in number and in size before labour observed in two types of anaemia, i.e. pernicious anaemia of pregnancy and vitamin C deficiency anaemia, is a symptom of serious

prognostic importance likely to be followed by a post-partum haemorrhage

(4) Eight cases of probable vitamin C deficiency anaemia of the present series, and 2 cases of vitamin C deficiency anaemia from a second series without any clinical evidence had the same blood picture as that found for scurvy in adults. The 2 patients in the second series could be identified as suffering from vitamin C deficiency anaemia because of their regeneration after high dosages of ascorbic acid and a relapse after reduction of those dosages.

(5) In view of the high incidence of anaemia in pregnancy in the 94 cases discussed and the tendency to further serious deterioration in the last 3 months of pregnancy, it would be advisable to make a full blood test in each 3 months period of pregnancy and also in the last weeks before labour.

My thanks are due to Dr H E Magee, Medical Officer of the Ministry of Health, for criticism and advice, and to Dr I A Scott, Medical Officer for the Metropolitan Borough of Fulham, for permitting me to give an account of these cases and for help throughout the work, and also to Miss M Abrahams, late Dietitian of St Bartholomew's Hospital, for assistance in preparing the paper for publication.

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Neonatal Mortality

B1

F M B ALLEN, M D , F R C P , C H G MACAFEE, M B , F R C S , F R C O G ,
PROFESSOR J H BIGGART, M D , D Sc

From the Royal Maternity Hospital, Belfast

This paper formed the basis of a discussion on neonatal mortality in the Ulster Medical Society in March, 1943

It analyses the neonatal mortality of 6,314 babies born in the Royal Maternity Hospital Belfast (ALLEN) 943 babies attended in private practice (MACAFEE) and the findings at the postmortem examinations of 125 babies who died during the neonatal period (BIGGART)

F M B ALLEN

THE importance of improving the welfare of infants and the health of children must be placed in the forefront of the better health services to which we all look forward. The falling birth-rate makes the conservation of child life of genuine importance to the nation.

In Northern Ireland, in 1939, 260 babies died on the 1st day of life, 302 in the next 6 days, and 237 in the 2nd, 3rd, and 4th weeks—a total of 799 babies lost in the neonatal period. In England and Wales it is estimated that in any one year 17,000 babies die during the same period.

It is obvious that a field of fruitful activity is open for those who are anxious to achieve a reduction in this wastage of human life. That a reduction is possible is shown in Chicago where a neonatal death-rate of 53.4 in 1930 was reduced to 28.8 in 1940. During the same period in the State of Illinois the rate was reduced from 56 to 35.1.¹ This was achieved by providing an extensive paediatric service supervised by an authority interested in infant welfare and by the inspiration of an enthusiastic paediatrician.

The factors which influence the survival of the infant at various stages of its develop-

TABLE I²
Neonatal Mortality Rates

	England and Wales*	Scotland	Northern Ireland
1939	28.1	36.6	31.7
1940	28.83	37.3	34.8
1941	28.52	39.9	33.8
1942	26.99	35.1	34.9*

* Provisional rates

ment have been summarized in a memorandum.²

(1) HEREDITY

Those interested in eugenics stress the importance of heredity. Every family doctor recognizes the truth of the saying that "breeding always tells" and sees it exemplified time and again in the nursery of the newborn.

(2) CONGENITAL MALFORMATIONS

The importance of this factor as a cause of stillbirth and neonatal death will be noted later in this paper. As these malformations have their origin in embryonic life any possible reduction in the incidence of this factor is doubtful until research throws more light upon their origin.

(3) TOXAEMIC FACTORS

Syphilis Pre-eclamptic toxæmia

Diabetes

(a) *Syphilis* Routine Wassermann tests in the Antenatal Department of the Royal Maternity Hospital for some years revealed an incidence of more than 1 per cent of unsuspected syphilis. The war-time increase in the incidence of syphilis calls for more attention to the possibility of imperfectly-treated maternal infection. Biggart's figures, however, would suggest that syphilis, as a cause of death in the neonatal period, is not an important factor.

(b) *Pre-eclamptic toxæmia* There is a possibility that pre-eclamptic toxæmia may adversely influence the welfare of the infant in intra-uterine and neonatal life. A dogmatic statement on this cannot be made in the light of our present knowledge, but personal observation lends support to this view. This type of toxæmia does, however, increase the number of premature infants and a large percentage of the mothers of these babies have difficulty with breast feeding.

(c) *Diabetes* This is an important factor in some cases of intra-uterine death and there is a high mortality among the babies of diabetic mothers in the 1st week of life.

(4) THE PREMATURE AND IMMATURE INFANT

For the purpose of uniformity all infants weighing less than 5½ pounds at birth are regarded as immature, irrespective of their estimated maturity. The well-recognized relation of immaturity to neonatal deaths is strongly borne out in this paper.

(5) NATAL CONDITIONS

These conditions are mainly the concern of the obstetrician and include birth trauma, respiratory distress, etc.

(6) POSTNATAL CONDITIONS

Lack of adequate skill, especially for premature babies, inability or lack of desire to breast feed and the failure to protect the infant against infection are important factors in accounting for neonatal mortality. From a paediatric standpoint factors influencing lactation are imperfectly understood and further information is urgently desirable.

TABLE II
Neonatal Deaths in Royal Maternity Hospital Belfast

Mature babies			
	Born	Died	Mortality rate
1939	1198	14	1.17
1940	1399	20	1.43
1941	1538	11	0.72
1942	1516	23	1.51
Total	5651	68	1.2
Immature babies			
	Born	Died	Mortality rate
1939	149	27	18.1
1940	131	38	29.0
1941	178	29	16.3
1942	205	49	23.9
Total	663	143	21.5

A detailed analysis of the deaths during the 4 years 1939-42 has been carried out. During this time 6,314 babies were admitted to hospital nurseries.

5,651 were mature and 68 died (mortality 1.2 per cent).

663 were immature and 143 died (mortality 21.5 per cent).

A postmortem examination was not made in all cases, in a few because the reason for death was obvious either from the clinical history or the physical examination (spina bifida, intracranial haemorrhage,

etc.) in others the provisional diagnosis was confirmed at necropsy, in the remainder the explanation of death was only revealed in the postmortem room. In passing it should be noted that in many cases the recorded cause of infantile death is inaccurate and unconfirmed by post-mortem examination (Spence, Miller²). Tables III and IV, however, present a picture of neonatal pathology as experienced in the Royal Maternity Hospital and show the importance of developing this field of pathological research.

TABLE III

The cause of death in 68 mature babies was

Congenital malformations	27
Intracranial haemorrhage	15
Infection	9
Respiratory distress	5
Erythroblastosis foetalis	3
Haemorrhage neonatorum	1
Mongolism	1
Renal thrombosis	1
Undetermined	6

TABLE IV

The cause of death in 143 immature (premature) infants was

Prematurity	76
Infection	15
Congenital malformations	16
Intracranial haemorrhage	11
Respiratory distress	15
Mongolism	2
Erythroblastosis foetalis	1
Haemorrhage neonatorum	1
Undetermined	6

The large number of congenital malformations accounting for neonatal deaths was somewhat surprising. Out of 211 (i.e. total neonatal) deaths 43 (20.4 per cent) were attributable to this cause (39.7 per cent in mature babies and 11.2 per cent in immatures).

This is not the occasion to record the number of stillbirths associated with congenital malformation, but it is possible that a similarly high figure would be found.

TABLE V

Nature of Congenital Malformation

Spina bifida	19
Meningocele	2
Hare lip, cleft palate	2
Alimentary	8
(Including oesophageal atresia, duodenal occlusion imperforate anus)	
Hernia of diaphragm	3
Ectopic vesicae	1
Congenital heart disease	8
(Including patent ventricular septum, patent foramen ovale and coarctation of aorta)	

The outstanding observation as regards deaths is that prematurity accounted for 76 of the 143 deaths among immature infants (53.1 per cent) and for 76 out of 211 total neonatal deaths (36.01 per cent).

TABLE VI

Deaths of 143 Immature Infants Related to Age at Death

Survival	1	2	3	4	5	6	7	8	9	10	11	12	or more days
No of deaths	73	18	4	5	7	4	2	2	2	0	0	0	26

This indicates clearly that the first two days, and especially the first day, are the most critical as regards survival and if an immature infant can be kept alive for the first 48 hours its prospects are greatly improved. The 26 deaths occurring on the 12th or subsequent days are mainly those due to congenital malformations and neonatal infection.

THE ROLE OF INFECTION

More than 11 per cent of the deaths were due to neonatal infection (9 among mature and 15 in immature babies). The role of infection as a cause of death in the newborn is not appreciated as it should be, this is the more regrettable since it is largely preventable. There is a tendency sometimes to attribute to innocent causes deaths which postmortem examination reveals as being

due to neonatal sepsis. An asphyxiated baby may be presumed to have died of asphyxia neonatorum when it really had neonatal pneumonia, or of severe icterus when septic cholangitis was present.

NATAL CONDITIONS

Birth trauma (usually intracranial haemorrhage) and respiratory distress accounted for 46 out of 211 deaths (21.8 per cent). The term respiratory distress is used in preference to asphyxia neonatorum and includes asphyxia from central causes, respiratory obstruction and atelectasis, injudicious premedication and rarer causes incidental to birth, such as interference with the umbilical vessels by knots and twists.

It is admittedly difficult to account for neonatal asphyxia in all cases, the factors to be considered are cerebral damage, neonatal pneumonia or atelectasis and congenital heart disease. Necropsies have been particularly useful in elucidating the cause of death because physical examination of the newborn infant is never easy.

THE REDUCTION OF NEONATAL MORTALITY

Research in the future may provide information concerning the occurrence of congenital malformations. Obstetricians are aware of the deaths which are directly associated with birth. Better obstetric practice should reduce the incidence of birth trauma, particularly intracranial haemorrhage, and in some cases prevent respiratory distress. An attempt should be made to advance the maturity of the infant as far as possible without prejudicing the safety or welfare of the mother.

Special attention has been given to the care of immature and premature infants in the Royal Maternity Hospital in an attempt to lower the mortality among them which at one time was over 40 per cent. To achieve

the reduction certain principles were observed and a routine was established. Especial care is taken in the labour room to avoid chilling of the infant so that abnormally low body temperatures do not occur. A specially trained nursery staff was appointed, the aim being that the nurse in charge should be prompt to recognize the failure to respond to treatment and be competent to apply the special measures necessary. The nursing staff is under the charge of a specially-trained Sister, and it is noted that 'black periods' in the records usually coincide with a change in staff. A special nursery is set apart for immature infants, which can be kept at a higher temperature of about 78°F, here additional moisture is added to the atmosphere so that a humidity of 60 to 65 is attained. This maintains body warmth and avoids excessive fluid loss. For the smaller babies oesophageal feeding is almost the rule, for those who are able to nurse from a bottle for a short time before trying a modified feeding bottle, preferably of the Belcroy* type, is used. Breast milk is regarded as the most satisfactory means of feeding, various substitutes having been thoroughly tried and proved inferior. A "pool" of surplus breast milk from mothers in the hospital is available for the feeding of immature infants. Each infant is kept warm in a simple type of electrically-heated incubator. The baby is wrapped in sterile gamgee and cleanliness achieved by the application of sterile olive oil. Visitors are not allowed into the nursery and those whose duty necessitates their admission must wear an effective mask over the mouth and nose. Babies who show any indication of infection are immediately segregated.

Neonatal infection is next in importance to immaturity as a cause of death and in itself exceeds in number the deaths due to

* Bell and Croxdon London

or associated with the delivery of the baby. Therefore any steps which can be taken to overcome and avoid an acquired condition which is so fatal are surely worth while. In hospital the rule is to segregate immediately a pyrexial infant and to ascertain the cause—the upper air passages, the respiratory tract and the alimentary tract are the most common sites. Local infection of the umbilicus is sometimes associated with infective cholangitis, B coli pyelonephritis (often with malformation of the genito-urinary organs) and, on two occasions, B coli meningitis have been found. Cutaneous infections are troublesome and demand isolation, but as a rule they respond to local treatment. In an epidemic of pemphigus neonatorum some years ago 54 cases occurred with 1 death, the cause of the epidemic being eventually traced to a laundry maid, engaged in folding napkins, who was infected with impetigo. It has been found that the use of an effective mask by all those whose duty it is to enter the nurseries assists in reducing neonatal infection. It must be realized that the portal of entry of the infective agent is very often the respiratory tract and that adults may project infected droplets by talking, coughing or even breathing near an infant. Neonatal infection in private practice almost always occurs when no such precautions are taken. In the Royal Maternity Hospital the "mask rule" was relaxed, but after 2 weeks the nursing staff asked that it be reimposed because 7 babies developed pneumonia and of these 2 died. The rule was again relaxed (except for the premature nursery) for 18 months from 1940, nurses being placed on their honour to report if they had any respiratory infection. During these 18 months of the four-year period under review, 5 out of 6 fatal cases of pneumonia occurred, 5 out of 8 of gastroenteritis and 1 out of 2 of septicaemia.

Paediatricians are convinced that breast feeding is in every way superior to artificial milk preparations. Figures are available showing that morbidity is higher among bottle fed babies and that the mortality is several times higher. It is notable that apart from the occurrence of conditions such as pyloric stenosis, mental defect, etc., attendance of infants at the outpatient departments of children's hospitals, and in private practice, is almost confined to those fed on breast milk substitutes. It is tragic to record that doctors and nurses are often among those who advocate artificial in preference to breast feeding. In many cases the reason would appear to be the lack of appreciation of the necessity for natural feeding and knowledge of its proper management. It must be realized that the proper teaching of students, nurses and doctors should be undertaken by paediatricians who are familiar with the difficulties encountered. Until adequate instruction is widely given public health campaigns will not achieve a full measure of success. Weaning sometimes takes place in the 2nd or 3rd week of lactation owing to a temporary failure when the mother resumes her household duties. It can often be avoided by resorting to supplementary feeding for a short time pending restoration of the natural supply. Again, the young, less experienced doctor, filled with enthusiasm for the practice of breast feeding encounters at times the ridicule of the older generation, and is unable to contend with the misguided mother who is influenced by commercial literature or the advice (and even threats) of her friends, parents, or "in-laws".

Infant welfare centres should play a large part in instructing and advising mothers, especially those who are inexperienced. That a service of this kind is welcomed has been proved at the Royal Maternity Hospital where the mother is taught to feed,

bath and dress her own baby before discharge, and where there is an infant clinic for 'well' babies up to 6 months. There is, unfortunately, no assurance that the staffs of all welfare centres have sufficient knowledge or have gained experience by residence in or attendance at a maternity and a children's hospital. It is essential that the Infant Welfare Medical Officer should have held the post of Resident Medical Officer in a Children's hospital and a Maternity hospital (preferably teaching) for at least 12 months.

There is an increasing appreciation of the importance of the maternal diet in relation to the success of lactation and the infant's welfare. A clinical assessment of the mother's health and prenatal diet suggests that the better they are, the more satisfactory will be the infant's progress. Evidence in support of this is accumulating and should soon be available. It has been stated that "a well-balanced diet of 2,500 calories for the last 3 or 4 months of pregnancy and during the early lactating period will result in fewer stillbirths, less delicate newborn babies and better maternal lactation. Even the provision of one meal daily of 900 calories is of undoubted value."²

SUMMARY

(1) An analysis of neonatal deaths over a four-year period is presented. It emphasizes the proportion of deaths due to congenital malformations incompatible with life, and of the role played by prematurity as the chief cause of death among immature infants.

(2) Steps to reduce neonatal mortality include better care of the immature infant, avoidance of neonatal infection, maintenance of breast feeding, and instruction on the management of natural feeding.

(3) Obstetricians should delay the induction of premature labour as much as

possible (without prejudice to the mother's welfare) so that the infant may be as mature as possible at birth.

(4) There should be increased and improved welfare services, associated with better instruction of the undergraduate, the family doctor and maternity nurses, on infant management and hygiene.

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- 5 By courtesy of the Registrar General and Statistician Northern Ireland

C. H. G. MACAFEE

This communication deals with what one might regard as a selected group of the population, namely private patients, in contradistinction to Dr Allen's paper, which gives the figures of a large maternity hospital receiving patients from varied social strata.

Table I gives the gross figures for the whole group.

TABLE I

Patients	928
Babies	943
Stillbirths	20
Neonatal deaths	16
Death-rate per 1,000 live births	17.34
N.I. Same period (average)	33.5

In going through these figures I was struck with the difference between two groups, viz. the figures for the period 1926-37, and those for the period 1938-42.

I understand from the statisticians that one cannot arrive at any conclusions from

such a small series Nevertheless if the causes of the stillbirths and neonatal deaths in these two groups are analysed some interesting points arise

TABLE II

	1926 to 1937	1938 to 1942
Patients	504	424
Babies	513	430
Stillbirths	15	5
Neonatal deaths	12	4
Death-rate per 1,000 live births	24.04	9.48
N.I. same period (average)	33	34

TABLE III
Stillbirths

	1926-37	1938-42
Death in labour	6	0
Macerated foetus*	4	1
Anencephaly	3	2
Albuminuria and placental infarct	1	0
Entanglement of cord	1	0
Second twin	0	1
Cerebral haemorrhage	0	1
	15	5

Neonatal deaths

	1926-37	1938-42
Prematurity	6	0
Congenital abnormalities	3	1
Asphyxia	2	0
Cerebral haemorrhage	1	1
Enteritis	0	1
Acute streptococcal infection	0	1
	12	4

Summary —

	per cent	
Pre-eclamptic toxæmia (resulting in prematurity or maceration) * (One case of maceration not associated with pre eclamptic toxæmia)	11	30.5
Congenital abnormalities	9	25.0
Birth trauma	3	8.3
Neonatal infection	2	5.5

The occurrence of 6 deaths in labour in the first group seems very high The 6 deaths, however, resulted from the following conditions —

Placental praevia	2
Prematurity (3-4 weeks)	2
Breech	1
Unexplained	1

The occurrence of 9 cases of congenital abnormalities (accounting for 25 per cent of the total) shows an incidence which corresponds closely to that of Dr Allen's series and is high when compared with other areas For example, congenital abnormalities only accounted for 12 per cent of the stillbirths and neonatal deaths in the Rotunda in 1940-41

Of the 3 cases of cerebral haemorrhage, one was due to an error of judgment for which I was partly responsible, one occurred in an easy spontaneous delivery and in the third case the delivery was accelerated on account of a cord prolapsing while the head was being rotated from the occipito-posterior position The rapid delivery almost certainly caused the tentorial tear

The 2 cases of asphyxia resulted from the babies being left unattended in their cots sucking bottles of water

Of the 2 cases of neonatal infection one was acquired from 'the child's grandmother who insisted on visiting the infant while recovering from an acute streptococcal throat

Of the 27 stillbirths and neonatal deaths in the first group pre-eclamptic toxæmia resulting in a macerated or premature infant accounted for 11 deaths In this group the incidence of pre-eclamptic toxæmia necessitating induction of labour was 12.9 per cent In the second group prematurity does not figure as a cause of death The incidence of pre-eclamptic toxæmia necessitating induction of labour in this second group was only 4.9 per cent.

and in all but one case the induction of labour was carried out in or after the 36th week

Are there any factors which may have influenced the better results obtained in the second group?

While it is impossible to be dogmatic I think there are at least three factors which have had an influence. In the second group I certainly paid more attention to the patient's diet during pregnancy, and in all cases this was supplemented by iron, calcium and vitamin products. In the case of pre-eclamptic patients, apart from rest in bed, the rigorous dietetic treatment advised in the past has not been enforced.

There is another factor which, I think, is most important. This is, that unofficially, pregnancy has become a notifiable condition. At the present it is a great advantage to be an expectant mother. She receives priority eggs, milk, clothing coupons, from the earliest days of her pregnancy, and to obtain these she not only acquaints her doctor but unblushingly notifies her milkman, grocer and chemist. This results in the patient receiving antenatal advice and treatment many weeks before the average patient usually saw a doctor in the past.

That there are many advantages in this is undoubted and these advantages have been borne out by a paper recently published by Nixon¹ on "Diet in Pregnancy". He includes in his paper a table, part of which is reproduced

The comparison of my two groups reveals the third factor. I have noted that in the second group of cases prematurity does not figure as a cause of death. This does not mean that there were no premature babies in the second group. The great majority were born in two private institutions, in one of which the facilities for the care and nursing of premature infants are the best available in this area.

In the other the Matron takes personal care of all premature infants and is most successful in their management. The figures therefore represent the results of careful antenatal supervision, with attention and additions to the diet, the minimal amount of trauma at delivery and efficient nursing of the infant afterwards.

I think that all will agree that the results in any series of cases depend not only on the medical attendant but also on the intelligence and co-operation of the mother (especially in cases of toxæmia), the surroundings in which the baby is born and, most important, the nursing facilities available.

If my conclusions are correct they point to certain ideals for the future.

First, that adequate antenatal supervision not only entails the recognition and avoidance of obstetrical complications but also supervising and supplementing the patient's diet. Where financial circumstances do not permit of this diet being adequate it should be supplemented by the State, and in return for this assistance the

TABLE IV

	Stillbirths and neonatal deaths (calculated per 1 000 total births)
1 Cases receiving special foods	59
2 Cases not receiving special foods but attending antenatal clinics	71
3 Cases not receiving special foods and not attending antenatal clinics	92

patient should be willing to be supervised from the earliest days of pregnancy

Secondly, that adequate provision should be made for every class of patient in efficiently organized and supervised institutions where premature infants can be nursed. At the present time in the British Isles the scarcity of accommodation for maternity cases is a serious problem for all expectant mothers and those who attend them, and provision for the premature infants is so limited that many cannot receive the best possible treatment.

The question of pre-medication in labour being a danger to the infant has been raised. While the indiscriminate and injudicious use of sedatives in labour is dangerous, I cannot agree that one has any justification in denying the mother relief from pain on account of, what I have personally found to be, a problematical risk to the baby. My second group of cases was the more heavily and generally pre-medicated of the two and yet the results, as far as the baby is concerned, were better. I have had experience of over 500 cases in which the combination of barbiturates and large doses of scopolamine have been used and in one only have I ever thought that the pre-medication had any influence on the foetal mortality. This was in one unexplained death occurring late in the 1st stage of labour.

I am satisfied, however, that the use of morphia in any form during labour is dangerous to the baby as it is liable to increase the risk of respiratory difficulties.

Co-operation between a skilled anaesthetist and the obstetrician at any delivery is an important factor in the establishment of respiration and the prevention of asphyxia.

Professor Biggart's figures show that of the postmortem examinations performed on stillborn babies or those dying shortly

after birth, 18 per cent show some congenital abnormality which accounts for the foetal death. This figure does not include the obvious abnormalities such as hydrocephalus and anencephalus.

In Dr Allen's series foetal abnormalities, obvious or revealed at postmortem, as a cause of death, accounted for 20.4 per cent, and in my own series the figure was 25 per cent.

It seems, therefore, that an unexplained foetal death in any case in which sedatives have been used is more likely to be due to some congenital abnormality, e.g., cardiac or intestinal, rather than to the sedative used.

I feel that it is unfair to hold the bogey of "It is dangerous for the baby" over the mother in order to avoid the extra trouble entailed for both doctor and nurse when any form of sedative is used.

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J. H. BIGGART

The findings at postmortem in 125 consecutive cases are tabulated in Table I. While the series is too small to justify statistical analysis the high ratio of congenital abnormalities is worthy of note (18 per cent). The present material contains none of those apparent malformations of the central nervous system such as hydrocephalus, anencephalus, meningoceles, etc. It consists entirely of malformations of the viscera which of themselves initiated the series of events which resulted in death of the child. Congenital malformations of the heart (10), atresia of the oesophagus (2), oesophageal-tracheal fistula, diverticula of the colon with perforation, volvulus of abnormal intestines, large diaphragmatic hernias producing

atelectasis, have all been encountered. Many of these conditions are difficult to diagnose in the young child, and their presence can only be detected at post-mortem.

rupture of the ascending colon apparently of traumatic origin. The case of mediastinitis was secondary to an acute oesophagitis. It is of some interest that in the five-year period during which these cases

TABLE I
TOTAL POSTMORTEMS 125
Tabulated Causes of Death

Postmortem findings	No	1st week	2nd week	3rd week	4th week
Congenital abnormalities	23	14	6	3	-
Intracranial haemorrhage	20	20	-	-	-
Prematurity	13	10	1	1	1
Atelectasis	9	9	-	-	-
Infections (36)					
Pneumonia	15	4	3	6	2
Septicaemia	8	-	5	2	1
Peritonitis	3	1	1	-	1
Enteritis	4	-	-	3	1
Meningitis	2	1	-	1	-
Laryngitis (non diphtheritic)	1	-	-	1	-
Pyelonephritis	1	-	-	1	-
Empyema	1	1	-	-	-
Mediastinitis	1	-	1	-	-
Erythroblastosis	7	7	-	-	-
Renal venous thrombosis	6	-	4	2	-
Oedema of lungs	3	3	-	-	-
Malnutrition	2	-	-	-	2
Cerebral venous thrombosis	2	-	1	1	-
Jaundice	1	1	-	-	-
Trauma	1	-	-	-	1
Haemorrhage	2	1	-	1	-
Total	125	72	22	22	9

Intracranial haemorrhage, chiefly due to tentorial tears, accounts for 16 per cent of the total deaths. One case of intraventricular haemorrhage and one of pontine haemorrhage were seen.

Infective lesions constitute 29 per cent of the total, almost half being infections of the respiratory system. Those dying in the first week were due to aspiration pneumonia (4), *B. coli* meningitis, *B. coli* empyema, and faecal peritonitis with

were collected there has not been a single case of congenital syphilis dying in the first 4 weeks of post-natal life.

Cerebral marantic thrombosis has been seen in 2 cases. Even more interesting are the 6 cases of bilateral thrombosis of the renal veins. The occlusion of these veins was the only finding at postmortem. Evidence of sepsis was not obtained, and it would appear that they must be considered of marantic origin.

Erythroblastosis and Congenital Syphilis in a Newborn Infant

BY

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AND

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THE chance association of erythroblastosis and congenital syphilis in an infant recently born in the Simpson Maternity Hospital aroused much interest, not only because of its rarity, but also because of the difficulty of differentiating these two diseases which have so many features in common. Little was known about erythroblastosis until the last decade and most of the more severe cases with stillbirth or miscarriage were diagnosed as congenital syphilis. A history of congenital jaundice, hydrops or intrauterine death, in successive pregnancies, was regarded as strong confirmation of the diagnosis of congenital syphilis, and women with such an obstetrical history were frequently given prolonged courses of anti-syphilitic treatment in spite of negative serological tests for syphilis. Extensive research and increased publicity during recent years have greatly increased our knowledge of erythroblastosis and more general recognition has shown the disease to be commoner than congenital syphilis.

Recently, one of us (Henderson), in a paper entitled "Erythroblastosis or Congenital Syphilis?" analysed the principal clinical and pathological features of these two diseases and discussed the differential diagnosis. The valuable serological test for erythroblastosis was not mentioned as it had not passed the experimental stage when this paper was written. The test is dependent on the development in the mother of

anti-Rh agglutinins, Rh (rhesus) being a factor in the foetal erythrocytes which is inherited from the father. The test is proving of great value in the differential diagnosis of erythroblastosis when expectant mothers give a history of recurrent miscarriage and/or intrauterine death. In the case about to be recorded the mother's Wassermann and Kahn tests for syphilis and the serological test for erythroblastosis were all positive. The hydropic infant died half an hour after birth. The cord-blood taken at birth gave a positive Wassermann reaction. A postmortem examination seemed to confirm the provisional diagnosis of congenital syphilis, but the histological features resembled those of erythroblastosis much more closely than those of syphilis.

CASE RECORD

Baby U female, born January 21st, 1943
first child illegitimate.

History of mother. Age 21 years. Four months after the last menstrual period she complained of a sore on the left side of the vulva. A few weeks later she noticed a rash on the abdomen and thighs which disappeared after 2 weeks. It returned a month later and became so irritable that she could not sleep. A few weeks later she went to a doctor who observed a rash on the back and abdomen and diagnosed secondary syphilis. She was admitted to the venereal diseases ward of the maternity hospital on January 6th 1943. Examination on admission

showed what appeared to be the primary sore on the left side of the clitoris and condylomata lata on the vulva. A fading roseolar rash was noticed on the skin of the abdomen and thighs and there were small condylomata under the left breast. One rubbery gland was palpated in the left groin and a few small ones in the right groin. The spirochaeta 'pallida' was demonstrated in serum from a labial condyloma and also from a submammary condyloma. Wassermann reaction ++, Kahn reaction +++ Gonococcal fixation test -. One week after the commencement of treatment the rash had entirely faded and the condylomata had almost healed. About a month later after histological examination of the foetal tissues the blood was investigated for evidence of erythroblastosis. The erythrocytes were found to be Rh negative and anti-Rh agglutinins were demonstrated in the serum (+ +).

History of infant A female infant was born spontaneously 15 days after admission of the mother to hospital. It weighed 5 pounds 15 ounces. It showed pronounced generalized oedema with great ascitic distension of the abdomen. Wassermann reaction of cord-blood +. The placenta weighed 1 pound 9 ounces and was abnormally thick; it had a rather pale colour and showed multiple small infarcts. The infant died half an hour after birth.

POSTMORTEM EXAMINATION OF INFANT

General appearances A female infant weighing 5 pounds 15 ounces. There was a considerable amount of generalized subcutaneous oedema. The abdomen was greatly distended and the umbilicus protruded.

Head There was no intracranial haemorrhage. The leptomeninges were extremely congested.

Thorax Pleural sacs were healthy. Pericardial sac contained a slight excess of clear fluid. There were no subserous haemorrhages.

Lungs were very poorly expanded and contained only a little air in the anterior borders. Otherwise they showed nothing of interest.

Heart was a little dilated and was rather large in proportion to the size of the body.

Thymus gland was small.

Abdomen Peritoneal sac contained a very large quantity of clear yellow fluid.

Alimentary tract showed nothing of note.

Liver was a little enlarged, firmer than usual and of fairly normal colour but a little browner than usual. It was possibly very slightly tough to cut. The outer surface was smooth but showed a very slight tendency to granularity when put on the stretch.

Spleen was greatly enlarged, being full, 3 inches in length. It was of about the usual consistence and colour and not tough. The Malpighian bodies were invisible.

Kidneys and suprarenals showed nothing of interest.

Bones The bones at both knees were examined. Both fibulae, which were cut into, showed a relatively bright yellow line at the epiphyses which was very suggestive of syphilitic infiltration.

HISTOLOGY

Liver (Figs 1 and 2) Haemopoietic activity was very great. Some of the foci were mainly or entirely normoblastic but many were composed of large primitive erythroblasts. This feature was quite characteristic of erythroblastosis. The centre of every hepatic lobule showed an area of necrosis in which haemorrhage had occurred and all the liver cells had either disappeared or lost all nuclear staining. In the outer zones the liver cells were healthier but they showed separation in the columns while individual cells were distorted and variable in size, some being atrophied, some containing several nuclei. In the peripheral zones there was a slight but quite definite pericellular fibrosis, which was not detectable in the necrotic central zones. The liver cells contained a considerable amount of haemosiderin. Spirochaetes were not found after prolonged search of sections stained by Dobell's method.

Spleen The most striking feature was active haemopoiesis with many primitive erythroblasts. Fibrosis was not evident. The Malpighian bodies were small. These changes were characteristic of erythroblastosis and it was doubtful whether any syphilitic changes were present. No spirochaetes were found in sections stained by Dobell's method.

Blood Nucleated red cells were numerous. There were many normoblasts and numerous more primitive cells. Anisocytosis was a feature.

Bone (fibula) Syphilitic infiltration was not discernible in the region of the ossifying junction. The marrow was actively erythroblastic.



FIG 1

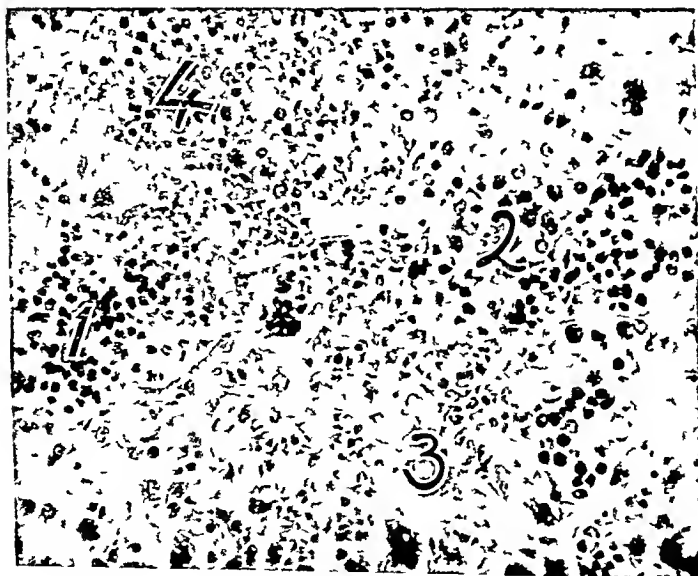


FIG 2

Lung Nothing abnormal was seen

Placenta The only remarkable features were slight stromal oedema and an excessive number of nucleated red cells in the vessels. Spirochaetes were not found in sections stained by Dobell's method

COMMENT

The evidence of erythroblastosis in this remarkable case is clear. Active haemopoiesis of a primitive type in the liver and spleen, central necrosis of the liver lobules, haemosiderin in the liver cells and erythroblastemia are all characteristic features. The pronounced generalized oedema with great ascitic distension of the abdomen, observed at birth, is more suggestive of erythroblastosis than of congenital syphilis, and the presence of anti-Rh agglutinins in the mother's serum strongly supports a diagnosis of erythroblastosis.

The evidence of congenital syphilis is less definite. The histological evidence, unlike that of erythroblastosis, is indefinite. The fibrosis of the liver, unrelated to the necrosis, and the distortion and atrophy of liver cells in the peripheral (surviving) parts of the lobules, were suggestive features, but in the presence of erythroblastosis as an alternative cause of fibrosis and in view of the failure to demonstrate spirochaetes, perhaps not conclusive. The failure to demonstrate spirochaetes is not vitally important, as they may be much scantier in viable than in macerated tissues and difficult to find in stained sections. They can seldom be demonstrated in the placenta in any circumstances. Infection of an infant's tissues with the spirochaeta pallida can be presumed when the mother is suffering from untreated secondary syphilis of several months' duration, and the infant's blood shows a positive Wassermann reaction, as in this case. The macroscopic

cal postmortem feature that most strongly suggested syphilis was the slight toughness of the liver, but this feature does not eliminate erythroblastosis, for a diffuse fibrosis is occasionally found in that disease also.

It is not surprising that a provisional clinical diagnosis of congenital syphilis was made in this case, in view of the florid untreated syphilis of several months' duration in the mother. In these circumstances, the hydropic state of the infant observed at birth and the very large spleen demonstrated at autopsy, though more characteristic of erythroblastosis than of congenital syphilis, did not create serious consideration of the former disease. Erythroblastosis was not suspected until the tissues were examined microscopically. The unmistakable evidence of erythroblastosis which this revealed led to the examination of the mother's serum for the presence of anti-Rh agglutinins. The demonstration of these antibodies confirmed the existence of erythroblastosis. If the presence of congenital syphilis should be regarded as unproven, the case loses little of its interest, for the clinical and macroscopic diagnosis of congenital syphilis appeared almost indisputable.

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LEGENDS

Fig 1 (1) Liver showing areas of necrosis and haemorrhage (2) fine pericellular fibrosis, distortion of liver cells and (3) haemopoietic foci

Stain H & E $\times 100$

Fig 2 (1) Liver showing foci of normoblasts and (2) primitive erythroblasts (3) liver cells containing haemosiderin granules and (4) margin of a necrotic area

Stain H & E $\times 100$

The Nomenclature of Hormone-Producing Tumours of the Ovary

BY

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SINCE gonadal hormones were first obtainable in pure form, our comprehension of them has extended widely and advanced with great speed. The newer knowledge shows that some of the current terms of pathology have questionable foundations and may perhaps convey misleading implications. Among such terms are those applied to ovarian tumours which disturb the manifestations of sex, namely 'arrhenoblastomata' and 'granulosa-cell tumours'.

ARRHENOBLASTOMA

The strict meaning of this name is, it may be supposed, a tumour arising from a masculine rudiment. Robert Meyer,¹ to whose careful investigation of these tumours we shall always be indebted, states "the fact that they can produce male characteristics, in my opinion, does not of itself furnish sufficient ground to call them arrhenoblastomas." Later he adds that "another reason for calling these tumours arrhenoblastoma of the ovary is based on the theory that, whether or not they produce male characteristics, they always arise from definitely male-directed cells," and "the resulting masculinization confirms the theory of the origin of this new growth." Here we have two possible fallacies, namely (1) that these tumours always arise from 'male-directed' cells, by which Meyer seems to imply male vestigial cells, and (2) that the resulting

masculinization confirms this assumption. Apparently it was thought that because the tumour caused masculinization it must, therefore, have been derived from a persistent male rudiment. However, as Meyer himself remarks, tumours which show the typical histological picture, namely the tubular adenomas, do not always cause masculinization or defeminization. Moreover Novak and Long have pointed out that ovarian tumours of diverse histological types may cause hairiness and other manifestations of virilism, although if sections from all parts of the tumour be examined "one can always find a suggestion of tubular or strandlike arrangement of the cells." Norris² states that "the term arrhenoblastoma must, in the present state of our knowledge, refer to a clinico-pathological condition, practically the term must be applied only when both the clinical and the pathological observations jointly justify its use." He says also that "there seems to be no justifiable morphological or genetic reason for deriving this neoplasm from any particular part of the primitive sex gland."

We arrive at these two conclusions (1) only some of the ovarian tumours showing the supposedly typical structure of a testicular rudiment cause masculinization, (2) tumours which do not show such a structure may yet cause masculinization. It seems that the ill-founded suppositions on which the term 'arrhenoblastoma' was

based are still maintaining certain erroneous ideas as though their truth had been established. In the light of present knowledge it would be rather a gross mistake to suppose that because a tumour produces androgen it therefore should have an architecture like that of the testicle. In the male, androgens are derived from the interstitial glandular cells of the testicle, which have no tubular or strand-like arrangement. This fact alone seems to destroy the foundation of the name arrhenoblastoma and to show that the term as defined in the authoritative literature is bound to cause mental confusion. Vestigial homologues of the vasa efferentia testis are commonly present in ovaries, and an excessive supply of androgen from any source will cause their hypertrophy, a tubular adenomatous structure in the ovary can, therefore, be explained as the consequence and not the cause of masculinization. Some ovarian tumours which induce hirsuties and other masculine phenomena are the colour of corpora lutea and are composed of cells which resemble those of luteal tissue, others might be described from their cytological appearance as thecomas, or as granulosa-cell tumours, and yet others look like tumours derived from adrenal tissue. In fact, by examining sections of an ovarian tumour under the microscope no reliable guidance can be obtained, either from their anatomical arrangement or individual appearance, as to the nature of the hormones, if any, which the cells may have produced.

Two reformations, it is suggested, might be made to render the terminology accord with fact. The first is to follow Ewing¹ and shorten the term arrhenoblastoma to 'arrhenoma' which means 'male tumour' and makes no assumption as to its origin in a testicular vestige, the second is to apply the term to all tumours, whether situated in the ovary, adrenal or elsewhere,

which produce excessive amounts of androgen and so bring about virilism. In this sense the name appears etymologically sound and carries an unmistakable meaning free from haziness and fanciful implications.

GRANULOSA-CELL TUMOUR OF THE OVARY

The objections to this designation are rather like those already adduced against the term arrhenoblastoma. Strictly the term is applied to ovarian tumours the cytology of which recalls the granulosa tissue of ripening follicles and the effects of which are those produced by oestrogen. In practice considerable latitude is shown and oestrogen-producing tumours of the ovary have been described as granulosa-cell tumours though their cytology would not support the title. According to Meyer¹ granulosa-cell tumours do not arise from the granulosa cells of ripening follicles but from undifferentiated cell rests. In some instances, though not in all, the tumours are accompanied by effects like those induced by oestrogen, including hyperplasia of the endometrium and enlargement of the mammae. "Thus," Meyer says, "we have both histologic and hormonal proof that these tumours arise from granulosa cells." Novak and Long² agree with Meyer that granulosa-cell tumours arise from cell rests and not from the granulosa of maturing follicles. They say "the granulosa cell is a typical feminine cell, producing the so-called female sex hormone." Against the term as currently used the writer would raise the following objections.

1 Those who have carefully investigated these tumours do not regard them as arising from the granulosa tissue of ripening ovarian follicles. If this opinion is correct the term 'granulosa-cell tumour' conveys a misleading implication.

2 It remains unproved that the granu-

losa cells of normal ovarian follicles form oestrogen, even if they do, they are not the only source. Granulosa tissue is readily destroyed by X-rays without causing other obvious injury to the ovary which will continue to form oestrogen though granulosa cells are absent.

3 Not every tumour which has the appearance of granulosa tissue will cause oestrogenic effects. Some are unaccompanied by evident hormonal disturbance, others cause masculinization.

4 Ovarian tumours composed of cells which do not resemble those of granulosa tissue may yet supply an excess of oestrogen.

From these facts the impediment which the term 'granulosa-cell tumour' offers to clear thought is apparent.

As a remedy the writer suggests that the term 'theloma' (female tumour) might be used to denote all tumours which cause an excessive supply of oestrogen, whether

they originate in the ovary, adrenal or elsewhere.

SUMMARY

Criticism is made of the terms 'arrhenoblastoma' and 'granulosa-cell tumour' and it is suggested that they might be discarded. It is proposed that the term 'arrhenoma' might be used to denote androgen-producing tumours and 'theloma' to denote those which produce oestrogen, irrespective of the location of the tumours in the body, or of their histological appearance.

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Spinal Anaesthesia in Cases of Delivery by the Obstetric Forceps

BY

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THE administration of spinal anaesthetics in obstetric conditions when Caesarean section or hysterotomy is necessary is recognized as a useful and beneficial method in suitable cases. The improvement in the solutions and in the technique employed has produced better results so that this method of anaesthesia is coming into more favour than formerly. Rufus Thomas¹ gives a very interesting review of 121 cases of Caesarean section done under spinal anaesthesia and discusses the advantages and disadvantages of the method. Other contributors to the literature on this subject, namely H K Ashworth,² S G Luker,³ K G Lloyd Williams,⁴ have commented favourably also on this method of anaesthesia for Caesarean section.

In the Glasgow Royal Maternity and Women's Hospital, spinal anaesthesia has been used for a long time routinely in one unit, and as an alternative method frequently for Caesarean sections and hysterotomies performed by other members of the staff.

The use of spinal anaesthesia in cases of delivery by the forceps has been found to be of benefit under certain conditions.

The cases in which this method would be found to be advantageous are

1 Deliveries following prolonged labour where there was 2nd stage delay and the patient was becoming exhausted.

2 Cases in which an anaesthetic had been already administered during the course of labour.

3 Cases of cardiac disease especially with an associated chest condition.

4 Cases of albuminuria or other constitutional condition in which a general anaesthetic, especially chloroform, would be contra-indicated.

The cases in which it would not be suitable are

1 The application of the forceps when the head of the child is high up and the uterus is contracted on an occipito-posterior position of the child. Manipulation to correct this position would be difficult or almost impossible.

2 Any abnormal presentation requiring intrauterine manipulation, e.g. internal or external version (for correction).

3 Any disease of the central nervous system or of the vertebrae or any septic condition at the site of the lumbar puncture.

In administering the anaesthetic the aim is to confine the anaesthesia so far as possible to the level which would affect the perineum and pelvic floor, i.e., a low spinal anaesthesia. It is not necessary to have the skin over the abdominal wall anaesthetized though, as a rule, the anaesthetic affects a narrow strip of skin above the symphysis pubis.

To achieve this result a small dose of a heavy solution is used with the patient in the upright position during the administration. The highest points of the iliac crests are taken and a line drawn between them passes over the tip of the 4th lumbar spine. Injection may be made in the space

above or the space below this point, the easier site being chosen

In the series of cases reported the earlier ones had planocaine 10 per cent (May and Baker), the specific gravity being 1032 and the later ones had the same preparation in 20 per cent strength with a specific gravity of 1040. The latter solution was found to produce the better result and a dose of 0.5 c.c. to 0.75 c.c. was found to be sufficient.

If blood-pressure is low ephedrine gr. $1\frac{1}{2}$ is injected intramuscularly but as the level of anaesthesia is low any alteration in blood-pressure would be no greater than with a general anaesthetic. The advantages of the method are

1 The general condition of the patient both during and after operation is much better than with a general anaesthetic

2 There is much less haemorrhage in the 3rd stage owing to better uterine retraction

3 The regional nerve block cuts out reflex stimuli from the perineum. This associated with the lessened haemorrhage removes the two main factors which are productive of obstetric shock

4 The anaesthesia would not produce or aggravate any pulmonary or toxæmic condition

In the management of the 3rd stage it is advisable not to administer pituitrin before the placenta has been expelled. It was noted that in those patients who had a spinal anaesthetic, pituitrin seemed to cause spasm of the cervix following delivery of the child so that the placenta tended to be retained whereas in those patients to whom pituitrin was not given the 3rd stage was of normal duration and there was no difficulty with the placenta. In the series of 60 cases conducted in this hospital, using spinal anaesthesia for delivery by the forceps, 30 cases were included from Professor Hendry's unit some time ago,

and the remaining 30 more recently from Professor Cameron's unit

The results were as follows

Parity	1st series	2nd series
Primigravidae	22	26
2 para	6	3
Others	2	1
	—	—
	30	30
	—	—
Ages	1st series	2nd series
Under 20 years	3	1
20 to 30 years	17	17
30 to 40 years	8	12
Over 40 years	2	Nil
	—	—
	30	30
	—	—

Indications for operative delivery

First series mostly 2nd stage delay

Duration of labour under 12 hours	2
12 to 24 hours	8
24 to 48 hours	11
Over 48 hours	9
	—
	30
	—

Second series

Primary uterine inertia	8
2nd stage delay	22
	—
	30
	—

Position of foetus	1st series	2nd series
Occip to anterior	15	8
Occipito posterior	8	6
Transverse arrest	7	14
		1 Breech presentation in primigravida
		1 Twins 1st vertex 2nd internal version to breech in primigravida
	—	—
	30	30
	—	—

Operations	1st series	2nd series
Mid forceps	17	20
Low forceps	13	8
Manual breech delivery	0	1
Twins (low forceps internal version manual breech delivery)	0	1
	—	—
	30	30
	—	—

Infants	1st series	2nd series
Alive	25	25 (2 showed signs of distress)
Stillbirths	3	3
Intrauterine death	2	2
	—	—
	30	30
	—	—

Maternal condition	1st series	2nd series
1 death		Good 25
Others satisfactory		Fair 3
		Unsuccessful 2
		—
		30
		—

Among the 60 patients there was only one maternal death, the case being of severe bronchitis with dyspnoea, in which a general anaesthetic was contra-indicated on account of the poor general condition of the patient. The child was stillborn and manual removal of the placenta was necessary. The patient collapsed and died 30 minutes after administration of the anaesthetic.

The cases of stillbirths occurred in infants in which a contributory cause was present either in the general health of the mother or in the duration of labour.

Otherwise the infants were in good condition and did not show any ill-effects from excessive compression by the uterine muscle.

In the second series a manual breech delivery of an infant weighing over 6 pounds was carried out successfully with-

out difficulty, also in a case of twins the second infant was converted by internal version from a vertex to a footling presentation and delivered without difficulty, the first child having been delivered by the forceps. Both patients were primigravidae.

The cases of occipito-posterior and transverse position were converted to anterior positions without undue difficulty before application of the forceps.

SUMMARY AND CONCLUSIONS

Sixty cases of operative delivery using spinal anaesthesia are reported and the results in two separate units have been shown in the various tables. Fifty-eight patients were delivered by the forceps, one case of twins by the forceps and internal version followed by manual breech delivery and one case of breech presentation delivered manually.

From the maternal aspect the parity and age group of the patients have been shown, also the indication for operative delivery and the type of operation.

With regard to the infants in the cases quoted the position *in utero* has been noted and the results as regards live and stillbirths.

The conclusions which one may draw from reviewing the cases in both series are that while low spinal anaesthesia would not be advised as a routine method it could be used with advantage in many deliveries by the forceps. Cases which would be unsuitable are those in which intrauterine manipulation to correct the position of the child might be difficult even under general anaesthesia.

The condition of the mother both during and after delivery compares favourably with that under general anaesthesia and in the 3rd stage the loss of blood is much less. In cases in which there might be contra-indications to general anaesthesia the spinal

anaesthetic would overcome the difficulty

I wish to express my thanks to Professor Samuel J Cameron and to Professor James Hendry for permission to carry out this method of anaesthesia in their units, also to the Registrar, Dr Matthew Garrey for his co-operation

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Onyala: A Tropical Condition Characterized by Haemorrhages Its Gynaecological Aspects

BY

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THE features of the condition known as Onyala are not to be found recorded in the textbooks of medicine generally used in temperate climates. It is of most interest to the physician but there are certain aspects of Onyala which are worthy of mention in a journal limited to the study of obstetrics and gynaecology.

In order to give the reader some idea of the chief features of this disease it will be necessary to mention briefly the major medical observations which have been made on Onyala.

The word Onyala is used to indicate a haemorrhagic disease, often fatal, which is characterized by the formation of bullae filled with blood in the mucous membrane of the buccal cavity and elsewhere. Most of the cases which have been described were recorded by workers in Central Africa, particularly in Portuguese West Africa. The disease is known to exist outside these territories, but it is very doubtful whether it exists outside Africa. In 1901 Preston Maxwell described a condition which occurred in certain parts of China; this condition appears to have certain points in common with Onyala. The cause of Onyala is not known. The subjects of the disease are young adults and men seem to be affected more often than women. Onyala has not been described in Europeans resident in tropical and sub-tropical countries.

CLINICAL FEATURES

Onyala develops suddenly. The initial symptoms are pains in the limbs and head-

ache; the temperature rises in the majority of cases. The worst cases are those which have a subnormal temperature.

The tongue becomes painful and colicky abdominal pain is often present. Bleeding occurs rapidly, that is, a few hours after the initial symptoms. Bleeding is most common from the nose and mouth, conjunctival haemorrhages are also frequently seen. Haematuria occurs in a large proportion of cases. The parotids tend to be swollen and tender.

Examination of the patient reveals the presence of haemorrhagic bullae which vary from the size of a pin's head to about a centimetre in diameter. Such bullae may be seen on the inside of the lips and cheeks, on the tongue, palate and fauces. The bullae also occur in the respiratory tract, in the intestinal and urinary tracts and extensive lesions are generally present in the skin. The bullae, which contain dark blood, break readily and this appears to be the cause of loss of blood from the organs mentioned above. The deeper tissues are also affected by Onyala. Haemorrhagic lesions arise in the lungs, the brain, the liver, and haemorrhagic effusion appears in the serous cavities. Haemorrhages may occur in the spleen; it is unusual for this organ to be enlarged in Onyala.

The course of the disease is very variable. Some patients have profuse haemorrhage from the nose and mouth, respiratory, intestinal or urinary tracts and death is rapid. In other patients the lesions are not extensive and there is only a slow ooze of blood; these patients generally recover.

Examination of the blood in cases of Onyala reveals a sudden fall in the red cells the resulting anaemia may be very severe. The blood platelets drop suddenly at the beginning, occasionally falling to less than 1,000 per c mm. There is a leucopenia and the reticulocyte count is low. The coagulation time is normal, but there is marked prolongation of the bleeding time.

If recovery takes place the platelet count rises rapidly and the bleeding ceases. The count does not reach normal until a few weeks have expired. When bleeding ceases the red blood cells start to rise in numbers.

Onyala is therefore considered by those who have studied this disease to belong to the group of purpuras it is regarded in the light of an acute thrombocytopenia.

In the present state of knowledge the treatment resolves itself into the administration of donor's blood. In the severe cases blood transfusion may be necessary, but in the milder cases intra-muscular injection of 20 c c of citrated blood given once or twice a day is usually sufficient. It may be necessary to continue the injections for 5 or more days. Calcium is often given, but it is not clear whether it is of much help.

- THE GYNAECOLOGICAL ASPECT

From the gynaecological point of view it is of interest to note that haemorrhage also takes place from the genital tract. In the few cases which the writer has observed, vaginal bullae were discovered on one occasion and these appeared to be the source of the blood-stained discharge. In another 2 cases blood was seen issuing from the external os. Not every case of Onyala in the female bleeds from the genital organs, this is true of both the severe and the mild types. Insufficient material has been seen to determine whether the uterine bleeding in Onyala occurs in the early or late phases of the

menstrual cycle. In one case in which the disease occurred in a multipara it was possible to obtain a small piece of endometrium for biopsy without unduly disturbing the patient. When examined microscopically the endometrial picture was typical of the first half of the cycle. There was diffuse haemorrhage in the whole of the small piece of tissue taken for section and it was impossible to see anything other than the normal arrangement of glands and stroma and interstitial haemorrhage.

Another patient (No 464, 1942) was sent into hospital from a country district. This patient was a young nullipara. On examination haemorrhagic bullae were found on the lips, on the tongue, the inside of the cheeks and in the skin. Blood was not present in the urine. The patient was losing profusely *per vaginam*, the loss necessitating the use of 16 pads a day. The temperature oscillated about 101°F. Examination of the blood showed that the platelets were reduced to 8,760 per c mm. Vaginal examination did not reveal any abnormality of the genital tract. There was no suspicion of pregnancy. The patient stated that she believed her next menses to be due about the time when she started to lose blood from the nose and mouth. Natives give notoriously bad histories and too much reliance cannot be placed on this. This patient was treated with intra-muscular injections of donor's blood and Coagulen Ciba. Recovery took place in 10 days, the loss of blood *per vaginam* ceasing about the 9th day. No history of excessive or irregular menses could be obtained. The stools and urine were examined and found to be free from parasites.

Onyala is not a common disease and it is decidedly rare for it to be seen during pregnancy. One case of Onyala in a pregnant multipara has been seen by the writer. In this case the symptoms devel-

oped about the 36th week of pregnancy. On admission the symptoms were found to be severe. treatment was carried out in the usual way. The foetus was alive and the pregnancy was normal so far as could be determined. On the 4th day of treatment the husband insisted on taking his wife to his kraal on the grounds that the time of delivery was near. The patient returned to hospital about 4 days later with severe bleeding from the nose and mouth and haemorrhages in the conjunctivae and skin. there was no vaginal bleeding. Examination revealed the foetus to be alive and the uterus felt normal to the touch. The patient was given a blood transfusion and the nose was plugged. Two days later labour commenced and progressed normally, a live baby being delivered. No excessive loss of blood took place during the 3rd stage of labour and the baby appeared to be normal in all respects. After delivery the mother's condition improved rapidly, bleeding from the nose and

mouth stopping on the 2nd day of the puerperium. No information could be obtained about subsequent events as it is impossible to "follow-up" native cases.

SUMMARY

Onyalai is a haemorrhagic disease of the nature of an acute thrombocytopenia. One of the symptoms may be bleeding from the genital tract, the blood may come from vaginal lesions or from the endometrium. In the solitary case in which Onyalai has been observed in late pregnancy it did not interfere with the pregnancy or the labour.

Although the disease has so far attracted attention only in Central Africa it is possible that it occurs in other places with similar climatic conditions, such as some parts of Central and Southern America. The description of these cases may induce others who have made similar observations in other countries to record their findings.

Fibroma of the Ovary with Ascites and Hydro-Thorax

BY

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THE presence of a pelvic tumour associated with ascites and pleural effusion is immediately suggestive of inoperable growth. That such a syndrome may exist with a benign and easily operable neoplasm of an ovary, it is important to recognize. Only 17 such cases have been described in the literature making 18 with that to be reported. This would suggest great rarity. It is more likely, however, that many others exist. Some of these may well have been denied operation when the existence of the syndrome was not recognized.

The first case was reported by Cullingworth¹ in 1879. There is no further reference till 1923 when Hoon⁴ of the Mayo Clinic reported 2 cases. Meigs^{8, 9, 10} in 1934 referred to 3 cases, reported a 4th in 1937 and subsequently collected 17 from the literature and from personal communications.

Rhoads and Terrell¹¹ first used the term "Meigs' Syndrome" when reporting a case in 1937.

SYMPTOMS

In the majority of cases the main symptoms were referable to the chest. The chief complaints were of shortness of breath, fatigue, cough and pain in the chest.

PHYSICAL EXAMINATION

There was usually considerable emaciation and evidence of loss of weight and dehydration. There may be some relation

between this dehydration and the rapid re-accumulation of fluid observed after tapping. The fluid in the chest was most often on the right side. In 3 of 18 cases it was on the left. One side only would appear to be affected. There was no relation between the side of accumulation of the fluid and the ovary involved.

The tumours are not massive ones, so that in the presence of much ascitic fluid it may be difficult on physical examination to determine that one is dealing with a smooth rounded mobile ovarian mass.

CLINICAL, PATHOLOGICAL FINDINGS

The specific gravity of the fluid varies between 1.013 and 1.018. Evidence of tuberculosis has not been found on guinea pig inoculation.

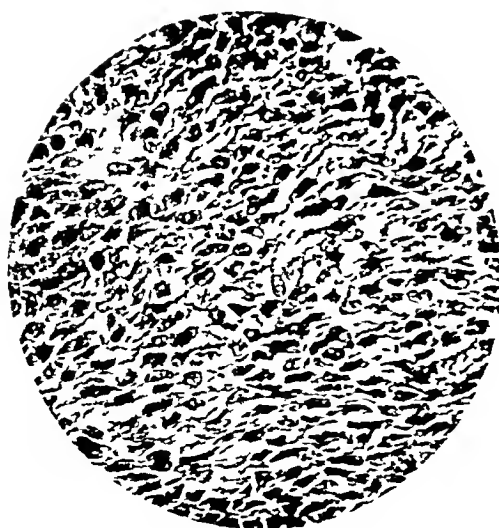
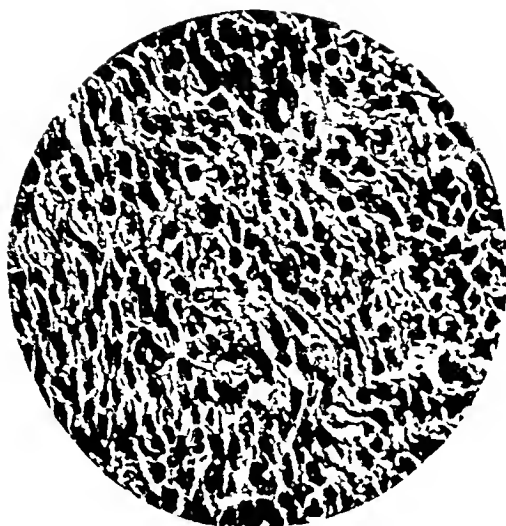
Only in the case here reported was there a high eosinophil content in the pleural fluid.

OPERATION

In most cases the chest was tapped before operation. Simple removal of the tumour is all that is called for. All the cases operated on have recovered and the hydrothorax and ascites rapidly and permanently disappeared.

PATHOLOGY

The tumour in each case was a typical fibrous connective tissue tumour with many collagen fibres.



CASE REPORT

W C a married woman aged 30, was admitted to hospital complaining of cough, shortness of breath and loss of weight over a period of 2 months. She also had pains across the abdomen and attacks of diarrhoea. Her bowels had previously been regular. Menstruation had always been regular with a normal loss lasting 5 or 6 days every 28 days but she had missed her last period which should have appeared a fortnight before admission. There had not been any pregnancies.

On examination the patient was seen to be very emaciated with sunken eyes, hollowing of the cheeks, lax skin and pasty complexion. The pupils reacted to light and accommodation. There was no abnormality in the neck other than that the trachea was slightly away from the mid line to the left. There was lessened movement and vocal fremitus was decreased on the right side of the chest. The percussion note was dull anteriorly and posteriorly and breath sounds were absent on the right side. The pulse was regular. The apex beat was situated in the 5th intercostal space a half inch lateral to the nipple line. The heart sounds were normal and the blood-pressure was 110 systolic 75 diastolic mm of mercury.

The abdomen was very distended with eversion of the umbilicus and dullness in the flanks which changed on movement. A mass could be felt arising from the pelvis on the right side for a height of 5 cm above the inguinal ligament.

On vaginal examination there was a hard mass in the posterior and right fornices but the body of the uterus could not be made out separately from the mass, nor could the mass be moved on bimanual examination.

On rectal examination a mass could be felt high up on the right side.

An X-Ray of the chest showed a massive effusion on the right side. After aspiration of 1500 c.c. of fluid and replacement with air some re-expansion of the lung occurred. X-Ray of the re-expanded lung did not show any evidence of secondary deposits. The pleural fluid was opalescent and contained an excess of cells of which a few were endothelial, the remainder leucocytes. Eighty-two per cent of these white cells were eosinophils, 14 per cent leucocytes and 4 per cent mast cells. The fluid was sterile on culture and tubercle bacilli could not be detected in film or culture.

Examination of the blood showed a red cell count of 4,060,000, haemoglobin of 60 per cent (Haldane) and colour index of 0.7. Differential white count showed a neutrophil leucocytosis of 89 per cent but there was no increase in the total white cell count.

Operation was performed under cyclopropane anaesthesia through a mid line suprapubic incision. A considerable volume of clear yellowish ascitic fluid was sucked away. The small bowel was collapsed and injected and some of the loop which had been lying in the pelvis were matted together with filmy adhesions of partly organized coagulated exudate.

There was a smooth shiny, whitish mass 25 cm. x 20 cm. x 15 cm. attached by a short pedicle to the posterior aspect of the right broad ligament. On the surface of the mass the flattened right ovary was seated.

The pedicle was clamped, divided and ligatured. So far as could be determined, by passing a hand above and behind the liver, there was no hole in the diaphragm.

Convalescence was uneventful. There was no further re-accumulation of ascitic fluid and 3 weeks after operation the fluid had disappeared from the right side of the chest.

The section of the tumour of which a microphotograph is reproduced was examined by Dr J. R. Gilmour who reported: 'A spindle celled fibroid-like tumour. A normal ovary was attached to the growth suggesting an origin in the mesovarium. The growth was very cellular but mitoses were rare, probably a fibroma.'

Six months after the operation the patient was enjoying normal health and X-ray of the chest showed normal lung fields.

COMMENTS

There are two interesting features of this case which do not appear in any of the 17 cases previously described in the literature. Firstly, there is the very high eosinophil content of the pleural fluid and secondly, the suggestion that the fibroma had arisen in the mesovarium.

A reasonable suggestion as to the origin of the ascitic or pleural fluid cannot be offered. Even if one were to accept the

explanation of an "irritative" effect of the fibroma on the peritoneum this still leaves the pleural fluid to be accounted for. The suggestion that a communication between peritoneal and pleural cavities through the diaphragm must exist, or that venous drainage of the pleural cavity by the azgos veins is interfered with, is entirely unsupported.

SUMMARY

1. The clinical features of the syndrome of fibroma of the ovary with ascites and hydro-thorax (Meigs' syndrome) are summarized.

2. Attention is drawn to the possibility of the syndrome being regarded as due to malignant metastases with consequent denial of operation.

3. A case of the syndrome is described.

ACKNOWLEDGEMENT

Thanks are due to Dr D H Irwin, Medical Superintendent, Essex County Hospital, Wanstead, for permission to publish the case.

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Soap as a Foreign Body in the Bladder

BY

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ACCORDING to Badenoch and Campbell¹ about a dozen papers are published every year on the occurrence of foreign bodies in the bladder. Tcherlok,² in an extensive review, found that foreign bodies were not usually introduced in attempts to procure abortion, but most of the cases among women reported from this country have been of this nature (Christie,³ Farncombe⁴ and Charles⁵). Foreign bodies in the bladder are almost always hard and coated with a phosphatic concretion, and their presence leads to haematuria, infection and severe pain on micturition. Numerous papers have appeared, mainly in the French journals, on the effect of intra-uterine injection of soap solutions (Yovanovitch,⁶ and Gross⁷), but we have not found any record of the introduction of soap into the female bladder. A woman has recently been seen in this hospital whose urine contained fatty acids and dissolved soap which, according to clinical observation, were present in the urine during its passage down the urethra.

CASE REPORT

An unmarried woman aged 20 years complained of pains in the back of 2 weeks duration with dysuria and frequency of micturition. Her recent history was of 'nephritis' in 1940 with haematuria and scalding pains on micturition but no oedema. In 1941 she was in hospital with pain in the right iliac fossa but there was no diagnosis. Early in 1942 she had pleurisy on the right side.

Clinical examination. The patient looked well

but appeared to be in pain. There was considerable tenderness on deep palpation of the lower abdomen on both sides, with some tenderness in the right iliac fossa. Rectal examination revealed tenderness apparently in the region of the junction of the right Fallopian tube and the uterus. Her menstrual history was of a 28-day cycle with 4 days periods which had recently been scanty and very painful.

Pathological examination. The blood urea and the chlorides, alkali reserve and protein of the plasma were normal and so was the blood count. The urine pH 6.5, contained albumin and uric acid bodies and a film of the deposit showed numerous Gram negative bacilli which on culture produced a heavy growth of *B. coli*. The patient who was not a virgin had no urethral discharge nor were there any signs of venereal disease.

Treatment. The *B. coli* infection was successfully treated by a week's course of Albucid (7.5 gm. per day) but the tenderness in the region of the Fallopian tubes continued, accompanied by a temperature which varied between 97°F in the morning and 103°F in the evening. Since this condition did not respond to sulphapyridine therapy a gynaecological examination under a general anaesthetic was performed but did not reveal any abnormality.

Fatty contaminant of urine. An oily substance which solidified on cooling had been noticed on the surface of the urine ever since admission and it was found that this substance was soluble in ether and chloroform. When crystallized from the latter solvent it formed whorls of needles melting at 36°C to 37°C which gave an acid reaction when pressed on wet litmus paper and liberated CO₂ from sodium bicarbonate solution. The crystals had a strong smell of scented soap and it was

suspected that they were a mixture of fatty acids. They were therefore dissolved in caustic soda acidified and the solution extracted with ether, evaporation of which yielded pale yellow needles melting point 31.5°C to 34.2°C setting point in melting point tube 28.0°C to 26.9°C equivalent weight 263. Acidification of the aqueous residue after ether extraction of the urine yielded a similar mixture of fatty acids equivalent weight 268.

Apparently the urine had contained floating droplets of free fatty acids, together with dissolved soap. Confirmation of this was obtained by the isolation of the fatty acids from a specimen of the patient's toilet soap. The odour and crystalline form were exactly the same as those of the substances isolated from the urine melting point 32.5°C to 39.5°C , setting point 32.5°C to 29.2°C equivalent weight 266. It is not surprising that the melting and setting points of the acids isolated from the urine should be somewhat lower than those of the fatty acids derived from the soap since the former were yellow in colour and would contain fat-soluble substances from the urine. The close correspondence between the equivalent weight of the fatty acids from the soap with that of the acids from the urine leaves little doubt that they were identical. The toilet soap did not contain any free fatty acid but after incubation at 38°C for 48 hours with urine (pH 5.5) the semi-solid floating matter when extracted with ether, yielded fatty acids of equivalent weight 243.

When the patient was deprived of her soap floating matter disappeared from the urine and a 24-hour urine specimen taken 2 days after the one which had yielded the results just described contained neither free fatty acids nor soap. The positive reaction for acetone bodies continued for about a week but as the food intake was abnormally low the acetonuria cannot definitely be correlated with the presence of soap in the bladder. The swinging temperature was eventually found to be associated with a hot water bottle under the patient's pillow. Examination by a psychiatrist gave no further information and the patient was discharged with a normal urine and temperature and without any abdominal pain.

CONCLUSION

The chemical evidence presented leaves little doubt that the floating matter found in the urine consisted of fatty acids derived from the patient's toilet soap. The hypothesis that this material came from the bladder rests largely upon the observation that the surface of the freshly-passed urine was covered with oily drops of colourless liquid resembling liquid paraffin, which solidified as the urine cooled. Soap incubated for 48 hours with urine swelled up considerably and was partially converted to fatty acids, but did not completely liquefy, so that the oily drops could hardly have been produced by dropping the soap into the urine after it had been voided.

SUMMARY

A case is described in which a patient is believed to have introduced toilet soap into her bladder. The soap was voided partly in the form of fatty acids which floated on the surface of the freshly-passed urine in the form of colourless oily droplets.

ACKNOWLEDGMENTS

Our thanks are due to Dr J. Mills for assistance in revision of the manuscript, and to Dr L. M. Jennings for permission to publish the clinical records.

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The Advantages and Disadvantages of Trial Labour

BY

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TRIAL labour is primarily intended for cases of moderate disproportion in primigravidae in which it is considered that, if the patient co-operates satisfactorily, the uterine action is efficient and the normal process of adaption of the foetus to the birth canal during labour is not disordered, delivery *per vaginam* will be practicable without undue risk of damage to mother or child. Its chief object is to minimize avoidable interference with normal course of labour.

This study is based upon a series of 127 consecutive cases of trial labour conducted

the true conjugate estimate was not recorded, in which the baby weighed less than 6 pounds, and in which a previous pregnancy had been carried beyond the 7th month were excluded. All patients had been examined during the late antenatal period or, in the few emergency cases, at the onset of labour, by the obstetrician in charge of the case.

The results observed are tabulated, for comparative purposes, with figures obtained from a series of 100 primigravidae without any evidence of disproportion.

	Cases	Stillbirths	Neonatal deaths	Maternal deaths	Notifiable pyrexia
Trial labour	127	3.1 per cent (4 cases)	2.4 per cent (3 cases)	0.8 per cent (1 case)	2.4 per cent (3 cases)
Normal labour	100	1 per cent	1 per cent	0 per cent	1 per cent

	Normal delivery	Instrumental delivery	Caesarean section	Duration of labour
Trial labour	53.5 per cent (68 cases)	31.5 per cent (40 cases)	15.0 per cent (19 cases)	31 hours
Normal labour	87 per cent	13 per cent	0 per cent	21 hours

in the Princess Mary Maternity Hospital during the past 7 years. About 20 to 25 per cent of the patients were under the care of Mr Frank Stabler and the remainder were my own. In order to form a basis for comparison, patients in whom the true conjugate was estimated to exceed $3\frac{1}{2}$ inches (whatever the size of the child), in which

From time to time objections to the procedure, of which the following are the most plausible, have been raised.

1. *The use of trial labour is a confession of failure on the part of an obstetrician who is unable to assess the degree of disproportion in his patients and therefore evades the*

issue by trying his luck with a course which will not commit him to a definite decision

This objection applies to the abuse and not the use of trial labour. Cases for trial must be selected with great care, and a patient must not be permitted to embark upon such a labour without a thorough investigation and careful assessment of the case. As, in spite of the most detailed examination, it is impossible to foretell with accuracy the fortitude of the patient, the efficiency of the uterine action or the precise mechanism which will operate during labour, the most rational way to find out how labour will progress in a border-line case of disproportion is to give a fair test. The selection of cases for trial and the management of labour have been discussed elsewhere.^{1 2}

2 *The teaching of methods of trial labour in medical schools may be misconstrued by some practitioners who, trusting to the trial to solve their problems, may neglect to examine their patients thoroughly before labour commences. After a short and inadequate trial labour such practitioners tend to lose confidence in their patients, and in themselves, and to perform that which is, only too often, an unnecessary Caesarean section.*

The choice of patients for trial labour and their management during the course of labour is outside the province of the general practitioner. Every patient should be under the immediate supervision of an experienced obstetrician who should assume sole responsibility for any decisions which may be necessary regarding the conduct or termination of labour. The selection of cases and choice of technique for Caesarean section is the duty of the obstetrician and not of a general practitioner or a general surgeon. The 15 per cent cases which require Caesarean section after trial labour might possibly have been delivered *per vaginam* had induction of premature

labour been performed in 100 per cent cases at the cost of the lives of babies

3 *The unfavourable psychological effect upon the mother of the death of her first baby after a long and distressing trial labour may have far-reaching consequences, and in these cases induction is valuable because, if the pregnancy is allowed to proceed to term, it is a matter of chance if the baby can be delivered alive.*

After excluding patients delivered by Caesarean section and those in whom the time of onset of labour was not recorded the average duration of the 1st and 2nd stages of labour in my trial cases was 31 hours compared with 21 hours in my normal cases. Peel³ records the duration of labour after bougie induction in 90 cases as 32 hours 49 minutes.

In my trial labour series the stillbirth-rate was 31 per cent and the ten-day neonatal mortality-rate 24 per cent. Townend,⁴ a supporter of premature induction, puts the combined foetal and neonatal mortality following this treatment for minor and moderate disproportion at 10 per cent, Bainster⁵ at 12.6 per cent, and Eden (quoted by Holland) at 14 per cent. Holland⁶ epitomizes the case against induction in the following words: "The whole-hearted exponents of induction spread their net wide. They are willing to induce many cases unnecessarily, in order to catch one in which the operation has been done at the proper time and has saved a Caesarean section or a craniotomy or a too difficult forceps extraction at term."

4 *Trial labour in domiciliary midwifery is not only worrying to the patient, distressing to her relatives and harassing to the nurse but noxious and exhausting to the practitioner in charge of the case.*

Trial labour should always be conducted in a hospital where facilities will be available for proper nursing attention, for effective antiseptic precautions and for any

operative procedures which may prove necessary during the course of labour. It is wholly unsuited to domiciliary practice. Peel replies to the last point in the words "If the doctor argues that he cannot afford the time to bear with the uncertainty these difficult cases often occasion, he is not a suitable person to deal with them."

5 *Delivery by the forceps is frequently necessary for the termination of trial labour.*

In my opinion the forceps-rate (in my series 31.5 per cent) is not unduly high in this class of case, and I think it is capable of considerable reduction by more frequent use of episiotomy during the 2nd stage of labour.

6 *The maternal morbidity- and mortality-rates in patients subjected to trial labour are high.*

In my series of cases the notifiable pyrexia-rate was 2.4 per cent and the maternal mortality-rate 0.8 per cent, figures which, in my opinion, are not excessive for cases of disproportion.

7 *Since the maternal mortality is known to rise the later in labour Caesarean section is performed the tendency will be to do it early, with the result that, instead of unnecessary inductions, there will be unnecessary Caesarean sections.*

Indications for Caesarean section during trial labour are lack of advance of the foetal head with the cervix more than half dilated in spite of satisfactory contractions an hour or more after rupture of the membranes, excessive moulding and caput formation without progress, and early evidences of obstructed labour. Signs of maternal or foetal distress becoming evident while the greatest diameter of the foetal head remains above the pelvic brim

sometimes hasten the decision, as may also increasing oedema of the cervix, disordered uterine action and lack of intelligent co-operation on the part of the patient. If these indications are taken as a guide, few unnecessary Caesarean sections will be performed, provided that the cases for trial have been properly selected.

8 *The educational value of labour following premature induction is as great as of trial labour at term and observations made during premature labour are equally helpful in arriving at a decision regarding the management of subsequent pregnancies.*

This sweeping statement bears no relation to the facts or even to reason. No true 'test' is involved in the average premature labour and the mechanism in such cases is atypical. It would be almost as rational to argue that, as a golf ball can roll into a standard hole, a biased bowl can do likewise.

I therefore conclude that trial labour is a justifiable and helpful procedure in cases of moderate cephalo-pelvic disproportion in the primigravida and that it is not attended by undue maternal or foetal hazard.

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A Case of Anuria Following Manual Removal of Placenta and Blood Transfusion with Subsequent Development of Irregular Heart Action Cured by Potassium Administration

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Mrs D aged 35 5-para whose previous obstetric history showed
 1935 Delivery by the forceps at term postpartum haemorrhage blood transfusion child alive and well
 1936 Five months miscarriage
 1938 Seven months birth Retained placenta and manual removal postpartum haemorrhage child died 1 day
 1940 Six months stillbirth retained placenta and manual removal postpartum haemorrhage

were given Group O, cross typed During the blood transfusion the patient was anaesthetized with ether and a manual exploration of uterus performed 2 hours 20 minutes after admission Placental shreds were removed with the finger and a hot intrauterine douch given Bleeding was not excessive Pitocin and ergotrate were given and the blood transfusion completed The pulse-rate after operation was 120, blood-pressure 86/48 later the pulse-rate rose to 140 and the blood-pressure fell to 60/35 Morphia gr $\frac{1}{4}$ was repeated and oxygen and coramine were administered Six hours later the pulse-rate was 122, and the blood-pressure 80/48, the improvement being maintained The following day she developed almost complete anuria which persisted for 4 days

During the antenatal period of the present pregnancy the patient was treated for pyelitis 4 weeks before delivery, being given 16 grm M & B 693 over a period of 2 weeks

She was admitted to hospital on August 2nd, 1942, having been delivered of a still-born child at her own home 8½ hours previously, she had a severe postpartum haemorrhage with retained placenta The placenta had been removed manually by her own doctor who, however, was not satisfied that he had completely removed it She was given 50 c c 50 per cent glucose intravenously, morphia gr $\frac{1}{4}$ and ergometrine and transferred to hospital

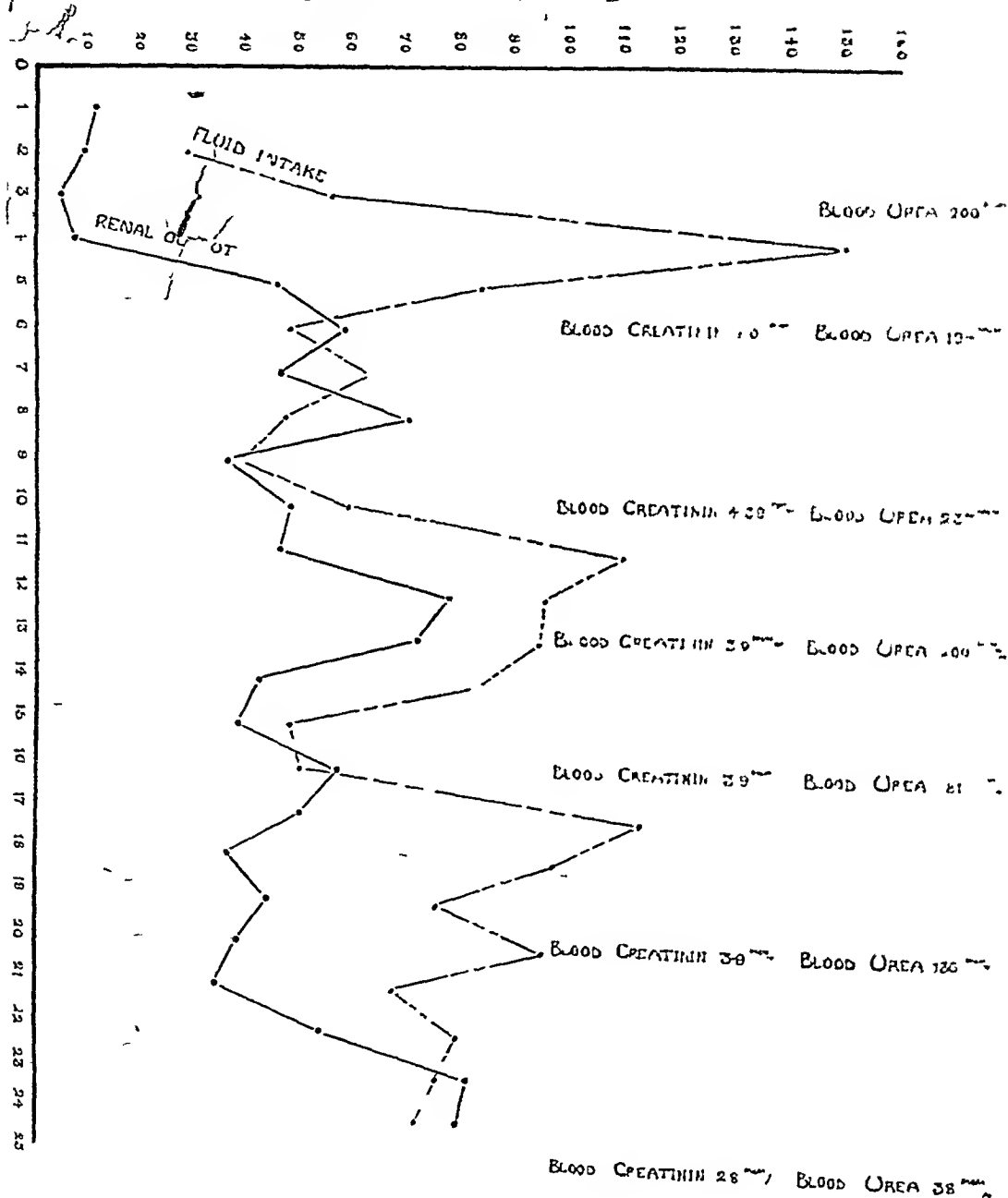
On admission 6 hours after manual removal her condition was poor, pulse 140, weak, blood-pressure 62/40, temperature 98.2, anaemic, faint icterus with only slight bleeding Morphia gr $\frac{1}{4}$, intravenous glucose-saline drip and blood transfusion

Day of puerperium	Urine passed in 24 hours	Fluid intake ounces
1st	12 ounces	
2nd	10 "	20-30
3rd	5	57
4th	8	151

The blood urea rose to 200 mg per cent on the 3rd day of the puerperium and 206 mg on the 4th day

On the 2nd day of the puerperium she was given 100 c c 50 per cent glucose solution intravenously On the 3rd day

CONCES OF FLUID



Fluid intake and renal output chart showing levels of blood urea and blood creatinin

continuous administration by the intravenous drip method of normal glucose-saline was commenced with 100 c c of 50 per cent glucose per 560 c c 5 per cent glucose-saline. A separate transfusion of 200 c c 43 per cent sodium sulphate was given. The drip was discontinued on the 6th day.

She was also given alkali orally in the form of sodium citrate and Tab Alk Effervesc Co (B W) but she was vomiting intermittently and it is doubtful if any of these drugs were retained. Antiphlogistine was applied to the loins.

On the 5th day urinary secretion recovered, the amount passed being 47 ounces in 24 hours. See graph of fluid intake and renal output, page 449. During this day 0.5 c c Salyrgan was given and repeated the following day. For the next 5 days although the urinary output averaged 50 ounces per day its urea content never rose above 1.10 gr per cent, the blood urea gradually rising to 237 mg per cent and the blood creatinin to 4.39 mg per cent. Some degree of pulmonary congestion had appeared but responded to atropine and digitalis. On the 9th day vomiting made it necessary to resume intravenous glucose-saline to maintain fluid intake.

Day	Intake (ounces)	Output (ounces)	Vomit (ounces)
5th	85	47	5
6th	50	60	-
7th	65	48	-
8th	49	72	18
9th	40	38	25
10th	61	50	10

Her general condition had now deteriorated. The stomach was washed out and sodium bicarbonate solution left in to allay vomiting.

On the 12th day her haemoglobin was 35

per cent, red-blood corpuscles 1,280,000 and white-blood corpuscles 11,000, and on the 14th day the intravenous glucose-saline drip was discontinued because of phlebitis, intravenous therapy having extended over 9 days. Two days later a rectal glucose drip was commenced. The urinary urea was still low, 0.75 gr per cent in concentrated specimen. Blood urea had fallen to 181 mg per cent and blood creatinin to 3.90 mg per cent.

On the 18th day her condition appeared hopeless, she was much weaker, complaining of headache and thirst. Her pulse-rate fell to 36, the heart action being very rapid and irregular. It now appeared that the myocardium was failing—the pulse-rate varying between 36 and 60. This failed to respond to cardiac stimulants.

Bearing in mind the physiology of heart muscle contraction it was considered that this irregularity might be due to an imbalance between Ca, K and Na ions in the plasma. Consequently on the 20th day 500 c c Ringer's solution was injected by the retromammary route and several hours later the pulse-rate was 72, the heart-rate and rhythm normal.

On the 21st evening the irregularity of heart had returned and calcium was then given in the form of Calcium Sandoz intramuscularly in 5 to 10 c c doses. No improvement in heart irregularity occurred.

On the 23rd day a further 300 c c of Ringer's solution was injected by retromammary route and 4 hours later the pulse and heart-rate and rhythm were quite normal. As large amounts of Na had been given in intravenous glucose-saline drip potassium was now administered in the form of potassium citrate and potassium bicarbonate grains 40 2-hourly. The following day the heart-rate and rhythm were regular and normal and remained so from that time onward.

After 2 days of the potassium therapy her

